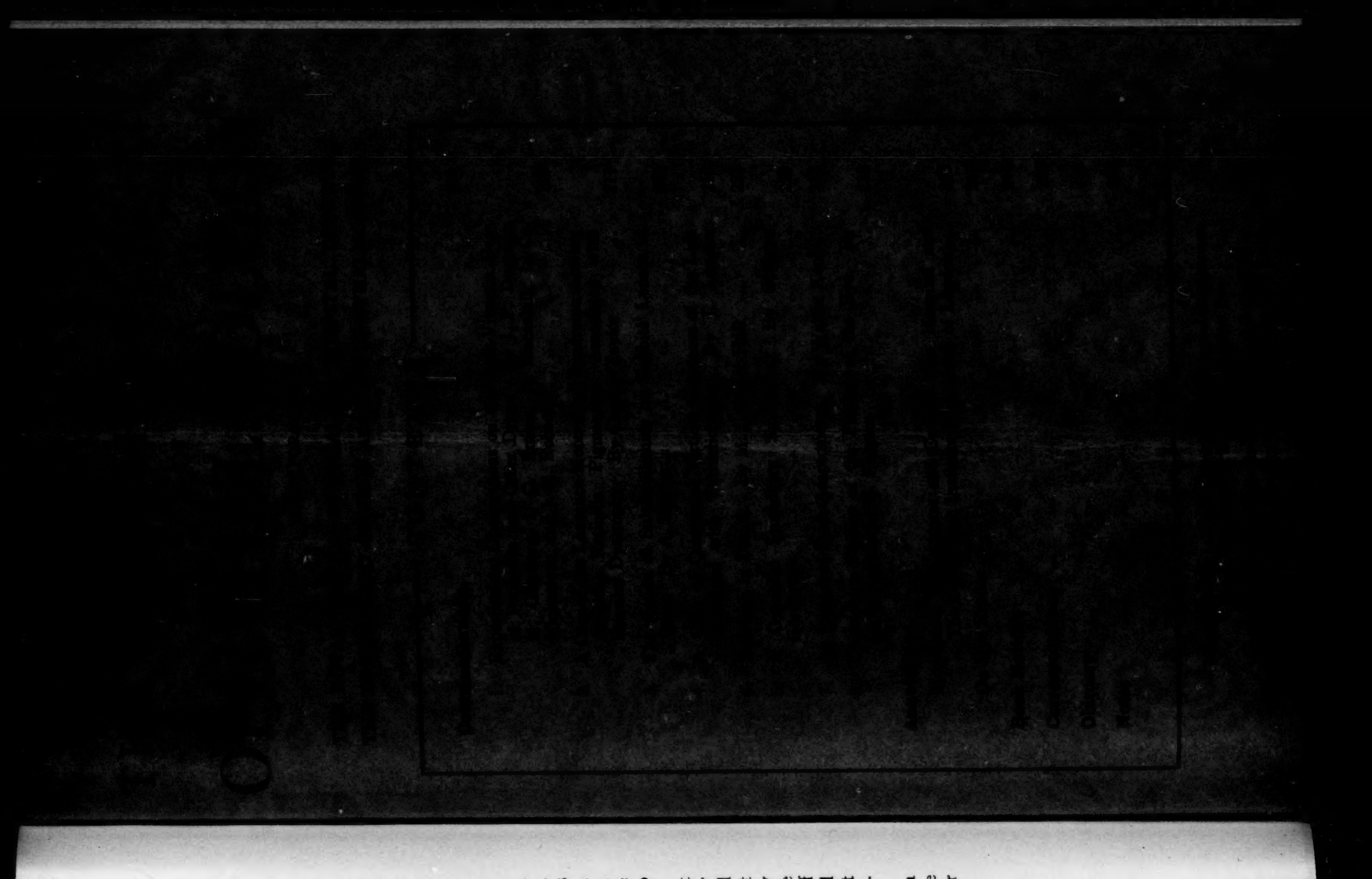

JOHN WEISS
287, OXFORD ST.
LONDON, 1913.

Trial Frame for both Spherical and Cylindrical Lenses, Independent P.D. Adjustments, Adjustable and Angling Sides, Bridge Adjustments for Height and Depth, Calls for Rotating Cylinders.

THE BRITISH JOURNAL

OF

OPHTHALMOLOGY

APRIL, 1947

COMMUNICATIONS

EXPERIMENTAL OBSERVATIONS ON THE INTRA-VITREOUS USE OF PENICILLIN AND OTHER DRUGS*

BY

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Introduction

IT is a matter of common experience that infection of the vitreous body is a major catastrophe which results almost inevitably in destruction of the eye. Interest, therefore, has been directed to new therapeutic agents which have been shown to be of value in the treatment of sepsis elsewhere in the body; in the hope that severe intra-ocular infection may also be controlled by them. Unfortunately, while drugs administered either orally or by injection readily reach most tissues in adequate concentrations, the vitreous is exceptional in this respect, in that drugs, present in the blood stream, do not easily diffuse into it. Hence, it is very difficult to produce adequate

* Received for publication, December 9, 1946.

concentration of therapeutic agents in the vitreous by their systemic administration.

It seemed desirable, therefore, to investigate the practicability of injecting these drugs directly into the vitreous, since it is known that they can produce their effect when applied locally to a site of infection. The experiments recorded below were made to this end and may conveniently be described under three headings. First, the effects of the drugs on the normal eye, secondly, diffusion of the drugs within the eye, and lastly, the value of certain drugs in the treatment of experimentally produced infections of the vitreous body.

METHODS

All experiments were performed on rabbits. Under ether anaesthesia the drugs were injected into the vitreous by means of needle puncture of the sclera in a region well behind the ciliary body, the needle being directed backwards to avoid possible injury to the lens. The needle used had a short bevell point, was 7-8 mms long and the amount of solution (0·05 or 0·1 c.c.) delivered by the syringe was accurately controlled by means of a micrometer gauge (see Fig. 1.).

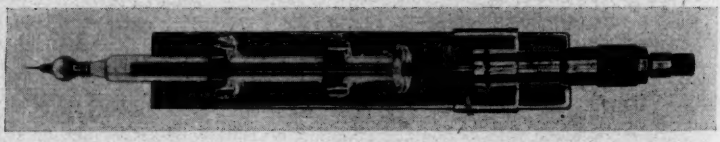

FIG. 1.

In most experiments a single injection was given, in a few the injection was repeated after 48 hours. Thereafter, the eyes were observed over periods of 10 to 128 days by the usual methods, particular attention being paid to the fundi and media. Finally, the eyes were removed and submitted to histological examination. The following drugs were used:—

1. Penicillin: Both commercial preparations (300-700 units/mg) and the pure sodium salt (1600 units/mg). The dose introduced was 2000 or 5000 units.

2. Sodium sulphacetamide: A 30 per cent. solution in pyrogen free water.

3. Marfanil: A 30 per cent. solution of Marfanil hydrochloride neutralised to pH 7·0.

4. V.335: (p-methyl sulphonyl benzylamine)—see Evans, Fuller and Walker (1944)—a 30 per cent. solution of the hydrochloride neutralised to pH 7·0.

Control experiments with normal saline were carried out.

Section 1. The effects of the Drugs on the Eye

METHODS

The effects of the drugs were observed on a total of 52 eyes of which 36 were examined histologically. Eight normal eyes, and 6 injected with saline were also examined histologically. Most of the material was fixed in 10 per cent. formol saline; that selected for examination by Nissl's method in 90 per cent. alcohol. While still in the fixative, the globes were divided equatorially and the posterior halves examined with a binocular microscope and the slit-lamp, and areas for section were selected. By this means, lesions seen and sketched in the living animal were identified and the correlation between clinical and histological findings ensured.

The tissues were embedded in paraffin, excepting those to be stained for fat, which were embedded in gelatin. All tissues were stained with haemalum and eosin; a few were in addition stained with scarlet red, with Nissl's stain, and with Marchi's method.

RESULTS

Great differences exist in the appearances of the fundi in apparently normal eyes of rabbits. While the usual appearance in pigmented animals is a fairly even granular one, not uncommonly pigment patches or clumps are seen, similar to those found in an old choroiditis in man. Histologically, however, such eyes do not show retinal abnormalities of the type to be described as resulting from the intra-vitreous injection of certain drugs. The vitreous opacities resulting from the injection of normal saline were slight and as a rule had almost completely disappeared after a week or two. No fundal changes were noted clinically in these eyes; in some examined histologically there were slight changes in the rod and cone layer which may have occurred post-mortem.

In 15 out of the 52 eyes infection was experimentally produced prior to injection of the drug. Histological changes in these cases were possibly products of both the drug and the infection and their significance was considered in the light of the changes found in those eyes into which only the drug had been injected.

COMMERCIAL PENICILLIN

Eight eyes were observed over a period of 10 to 29 days and 4 were sectioned. In only 1 eye had infection been experimentally produced. Opacities, sometimes dense, appeared in the vitreous body and remained until the end of the experiments. These eyes received a single dose of 2000 units or, in one eye, of 5000 units; or a double dose of 2000 units with an interval of 48 hours. The fundi

suffered damage in all cases. Below the medullated nerve fibre bundle pigmentary changes developed, and, in one case, this progressed to a retinitis proliferans with detachment. Three eyes showed fine new vessel formation with swelling of the medullated nerve fibre bundle, and retinal haemorrhages appeared in one of them. Posterior cortical lenticular opacities appeared once.

Histologically, in keeping with these findings, all the sectioned eyes show numerous monocytes in the posterior vitreous, large circumscribed areas of complete retinal destruction with glial replacement, and pigment aggregates in the retina resulting from disturbance of the retinal pigment layer. The vessels, which normally lie free on the medullated nerve fibre bundle, are embedded in a non-cellular matrix. This matrix is possibly a factor in producing the swollen appearance in the nerve fibre bundle seen ophthalmoscopically. No infiltrates or transudates are present within the retina, and the choroid is unchanged.

PURE PENICILLIN

Fourteen eyes were examined over a period of 10 to 27 days and 8 were sectioned. These eyes received a singe dose of 2000 units or of 5000 units of crystalline penicillin; or a double dose of 2000 units with an interval of 48 hours. In 4 eyes the penicillin was injected 6 hours after inoculation of the vitreous with haemolytic streptococci. Toxic effects, while present in many of the eyes, were much less than with the commercial preparations. In one eye there was swelling of the medullated nerve fibre bundle and in another opacities in the posterior cortex of the lens. Histologically 3 out of 8 eyes sectioned show areas of retinal destruction. This is in keeping with the findings of Sallmann *et alia* (1944) who found 4 out of 11 eyes so affected. The histological changes are more marked than the clinical appearances had suggested. For example, 2 non-infected eyes in which vitreous opacities were the only ophthalmoscopic changes show circumscribed areas of retinal destruction and in the lower periphery an accumulation of pigment in the rod and cone layer. These eyes received a single dose and a double dose of 2000 units of crystalline penicillin respectively and indicate the difficulty, repeatedly experienced in these experiments, of assessing cellular changes in the retina on the basis of the ophthalmoscopic appearances alone. In one eye there are numerous small pigment aggregates within the retina. The eyes receiving a double dose were more affected than the others. These findings show that crystalline penicillin, in the doses stated, can produce definite toxic effects on the retina. Nevertheless, the changes are not so marked as with the commercial preparation, and unlike the latter, crystalline penicillin appears to have no predilection for the vascular system.

SODIUM SULPHACETAMIDE

Of 16 eyes examined over a period of 10 to 128 days, 13 were sectioned. The eyes received a single dose of 0·1 c.c. of 30 per cent. sodium sulphacetamide or a double dose of that quantity with an interval of 48 hours. In 5 eyes the drug was given at one hour after the inoculation of the vitreous with haemolytic streptococci. Of the 11 eyes in which no infection was introduced the fundi of 6 appeared normal while in the others patchy changes of a mottled appearance developed in the lower part of the fundus. There were no notable changes in the retinal vessels. In all the sectioned globes there are circumscribed areas, varying in size, of complete retinal destruction in the lower part of the fundus, excepting the 5 eyes infected with haemolytic streptococci. As these latter eyes had been removed 10 days after the infection and the minimum period between injection and enucleation in the others was 75 days, it may be presumed that a definite period of probably several weeks is required for the development of areas of complete retinal destruction. The eye which received a double dose of the drug is more affected than the others and shows retinal detachment and cystic formation within the retina as well as an extensive area of destruction. Practically all the eyes (infected and non-infected alike) show fairly widespread changes at the level of the rod and cone layer as indicated by the presence of pale staining detritus and numerous large droplets. These appear to be the product of the rod and cone layer and not of the pigment epithelium as suggested by Koyanagi and Kinnikawa (1937) and von Sallmann *et alia* (1944). This change can be noted particularly in the retina adjacent to the atrophic areas already noted. In assessing the significance of this appearance it must be remembered that it may be noted in a lesser degree as a post-mortem change. In some cases the outer nuclear layer of the portions of the retina affected in this way shows diminution in the number of its cells, and in one case there is complete absence of the outer molecular layer in the area corresponding to the maximum degeneration of the rods and cones. It is noteworthy that the fundi of several of the sectioned eyes showing marked histological changes were clinically normal, as had indeed previously been found by Leopold and Scheie (1943). Beyond 100 days infiltration of the vitreous with monocytes is not a feature of any of the cases.

After 128 days 5 eyes which were stained for Nissl's granules, with Marchi's method and for fat with scarlet red, show no abnormalities in the ganglion cells, in the medullary sheaths or in the nerve fibre bundles. In no case was the choroid found to be affected.

The toxic effects of sodium sulphacetamide on the retina appear to be more severe than those of crystalline penicillin; and further,

there is a difference in that the areas of destruction with sodium sulphacetamide appear only after a delay of several weeks. With both drugs, however, the initial effect is apparently on the outer part of the retina. It is noteworthy that the media, including the lens, were clear in all cases after 128 days.

MARFANIL

Injections of marfanil were made in 5 eyes, 4 of which were sectioned. Each case received a single injection of 0·1 c.c. 30 per cent. solution or two such doses at an interval of 48 hours. In 2 cases the injection was preceded by the inoculation of haemolytic streptococci. The periods of observation were 10 to 17 days.

Vitreous opacities were slight. The most notable clinical features in all cases were constriction and, in places, variation in calibre of the retinal vessels which were often reduced to threads. Two of the cases showed swelling of the medullated nerve fibre bundle. One showed haemorrhages and new vessel formation. In all cases examined histologically there are circumscribed areas of retinal destruction and in many, pigment aggregates within the retina. In 2 cases there appears to be thickening of the retinal vessel walls.

Marfanil is more toxic to the retina than sulphacetamide or penicillin. Like impure penicillin it appears to have an effect on the retinal vessels and to cause pigmentation of the retina.

V.335

Injections of V.335 were made in 9 eyes of which 7 subsequently were sectioned. A single dose, or two doses at an interval of 48 hours, was given and in 2 cases the injection was preceded by experimental infection of the vitreous. The periods of observation were from 10 to 33 days.

Only slight opacities formed in the vitreous. Clinically all eyes had marked changes in the lower part of the fundus with obvious pigment disturbance. The vessels were not notably affected. Histological examination confirms the severity of the fundal changes. In all cases there are extensive areas of retinal destruction and 3 eyes show separation of the retina. In most there are marked disturbances of the rod and cone layer, similar in appearance to those already described. In 3 the choroid shows numerous foci of round cells, though none of these eyes had been infected. Both the clinical and histological findings indicate that V.335 is toxic to the retina and apparently to the choroid. Of all the drugs used and described in this report it appears to have been the most toxic.

Summary of effect of drugs on tissues of rabbits' fundus

(1) A study of these 52 eyes shows that all of the drugs used are capable of producing a toxic effect on the retinal cells. In

Table I the drugs are arranged in the order of the increasing severity of their toxic effects. It is obvious that crystalline penicillin is the least toxic of the 5 substances tested and V.335 the most toxic. Although it is possible to assess the vessel changes clinically, the assessment of retinal cell damage must be based on the eyes histologically examined. The number of eyes showing areas of retinal destruction is therefore expressed as a fraction of the eyes sectioned.

TABLE I

Showing certain toxic effects of drugs arranged in order of their increasing severity.

Drug	No. of eyes observed clinically	No. of eyes showing vessel changes in the fundus expressed as fraction of eyes clinically observed	No. of eyes showing opacity in posterior lens expressed as fraction of eyes clinically observed	No. of eyes sectioned	No. of eyes showing histological areas of retinal destruction expressed as fraction of eyes observed histologically	No. of eyes showing pigment aggregates in retinae expressed as fraction of eyes observed histologically
Crystalline penicillin	14	0/14	1/14	8	3/8	2/8
Commercial penicillin	8	3/8	1/8	4	4/4	4/4
Sodium sulphacetamide	16	0/16	0/16	13	8*/13	0/13
Marfanil ...	5	5/5	1/5	4	4/4	3/4
V. 335 ...	9	0/9	1/9	7	7/7	2/7

* The five eyes which do not show areas of retinal destruction were removed 10 days after injection, a period probably too short for development of these areas in the case of sodium sulphacetamide. Such areas of destruction were present in all eyes sectioned after 73 days.

(2) Although with all these drugs eyes are shown in which there are localised patches of retinal destruction in the lower part of the fundus, the initial effect especially with sodium sulphacetamide, appears to be on the rod and cone layer. This is suggested by the

eyes in which the only retinal changes were in the rod and cone layer, the presence of changes in that layer in the otherwise normal retina adjacent to foci of complete retinal destruction, the presence in several eyes of cystic and other changes in the outer nuclear layer, and the absence of changes in the inner retinal elements in several eyes specifically stained. Sallmann *et alia* (1944) have commented on the early involvement of the outer retinal elements following intra-vitreous injection of penicillin.

(3) Commercial penicillin and marfanil are capable of a toxic effect on the retinal vessels as indicated clinically by vascular constriction, calibre variation, and new vessel formation, and histologically in one or two eyes by changes in the vessel walls.

(4) In no case were there transudative or exudative changes present in the retina.

(5) The choroid was free from change in practically all eyes.

(6) Correlation between ophthalmoscopic changes if present and histological findings should be ensured by identification of the lesion in enucleated eyes with the help of the slit-lamp and the binocular microscope. No absolute statement regarding retinal cell changes of even a gross nature can be based on ophthalmoscopic examination alone.

Section II. The diffusion of the drugs within the eye

METHODS

The drugs were injected into the vitreous as described in Section I. After intervals varying from 1 to 72 hours, the animals were killed and certain tissues of the eye were removed for estimation of their drug content.

Sulphacetamide estimations were made on the aqueous, vitreous, cornea, iris, lens, chorio-retinal tissue and sclera, which were removed in that order immediately after the rabbit was killed. Following dissection, the tissues were washed rapidly in saline, dried on blotting paper and, after weighing, thoroughly ground in glass mortars with 2 ml. of 15 per cent. trichloracetic acid and silver sand. The macerated tissues were allowed to stand for 30 minutes, when the contents of the mortars were washed and filtered into 25 ml. measuring cylinders and the volume made up to 25 ml. Sulphonamide estimations were made by the colorimetric method of Bratton and Marshall (1939) in 10 ml. aliquot portions. Readings were taken on a Klett visual colorimeter and Spekker photo-electric absorptionmeter.

Penicillin estimations were made on the aqueous, vitreous and cornea. These tissues were removed from the rabbit and subsequently handled with aseptic precautions. The cornea was ground in an agate mortar with sand and with a certain measured amount

of nutrient broth; after standing for one hour, the broth containing the macerated cornea was centrifuged and the supernatant fluid taken for testing. The penicillin estimations were made by a serial dilution test; this determined the highest dilution of the eye fluids in nutrient broth which completely inhibited growth of the standard (Oxford) ***staph. aureus***. The particular dilutions examined in each instance were chosen according to the penicillin concentration considered likely to be present. The volume of the test mixture was usually 0·4 ml. Each tube was inoculated with a loopful of a 1 in 300 dilution of an eighteen hour broth culture of the standard staphylococcus. After incubation at 37°C. for about eighteen hours, the tubes were examined for growth as shown by the presence of turbidity. The presence or absence of growth was confirmed by a stroke-subculture on a blood agar plate. In control tests, it was found that the lowest concentration of penicillin completely inhibiting growth was between 1/20th and 1/25th of a unit per ml. For the purpose of calculating the penicillin concentrations in unknown fluids in terms of unit per ml., it was assumed that their highest bacterio-static dilutions contained 1/20th of a unit per ml. For instance, if growth of the staphylococcus was inhibited by the fluid diluted 1 in 20, but not by the fluid diluted 1 in 40, the penicillin concentration of the fluid was reported as being between 1 and 2 units per ml. (The eye fluids themselves, in the absence of penicillin, were not found to have any bacteriostatic effect in the dilutions tested).

RESULTS

(*a*) ***Injection of sodium sulphacetamide into the normal vitreous.***—Table II shows the concentrations of sulphacetamide found in the vitreous, aqueous, cornea, iris, lens, chorioretinal tissue and sclera, one hour, six hours, one, two, three and four days after the injection of 0·1 ml. of 30 per cent. sodium sulphacetamide.

It was found that the drug rapidly diffused into all the tissues which always contained high concentrations within an hour after injection. In the vitreous, the concentration fell from about 1000 mg. per cent. (*i.e.* per 100 gm.) at one hour after injection to an average value of 2·5 mg. per cent. after four days. Chemotherapeutic concentrations (*i.e.*, over 5 or 10 mg. per cent.) were usually found in all the ocular tissues after 2 days and sometimes, in the vitreous, even after 3 days. In Figs. 2 and 3, the logarithm of the average concentration of sulphacetamide has been plotted against the time after injection. In the vitreous (Fig. 2), the log. of the concentration fell in inverse proportion to the time after injection.

(*b*) ***Injection of sodium penicillin into the normal vitreous.***—Table III shows the concentrations of penicillin found in the vitreous, aqueous and cornea, one hour, six hours, one day, two days and

three days, after the injection of 2000 units of impure sodium penicillin into the vitreous. Table IV shows the results for similar experiments with pure crystalline sodium penicillin.

TABLE II

Concentrations of sulphacetamide in the ocular fluids and tissues after the intra-vitreous injection of 0·1 ml. 30% sodium sulphacetamide in the normal eyes of rabbits.

Time	Rabbit No.	Mg. Sulphacetamide per 100 g.						
		Vitreous	Aqueous	Cornea	Iris	Lens	Choroid and Retina	Sclera
1 hr.	1896 R.E.	1300	232	102	122	21·1	290	213
	1898A „	1300	69·3	51·6	183	28·3	250	212
	1910A R.E.	960	268	177	308	—	391	149
	1910A L.E.	980	342	257	440	—	351	198
6 hrs.	1896 L.E.	670	—	105	138	38·0	120	115
	1898A „	1080	218	180	263	61·7	254	121
	1911A R.E.	550	205	187	221	—	202	125
	1911A L.E.	810	275	203	253	—	287	197
1 day	1888 L.E.	209	92·5	94·0	106	—	—	71·7
	1888 L.E.	353	111	84·2	12·0	—	—	43.7
	1900A R.E.	310	49·9	70·0	36·6	38·5	41·0	—
	1900A L.E.	311	58·2	64·7	85·0	20·2	42·5	45·0
	1912A R.E.	201	20·5	20·7	—	—	—	—
	1912A L.E.	239	63·5	80·1	74·5	—	—	—
2 days	1887 R.E.	115·1	18·9	11·3	19·2	—	—	38·2
	1887 L.E.	70·9	—	7·0	14·0	—	—	10·1
	1901A R.E.	31·1	4·0	6·3	11·1	16·9	10·7	13·5
	1901A L.E.	25·7	3·5	7·4	12·1	13·9	9·6	7·9
3 days	1886 R.E.	23·7	4·9	2·8	3·0	—	—	2·0
	1886 L.E.	13·0	0·85	1·0	1·6	—	—	1·2
	1902A R.E.	1·5	0·5	1·0	1·0	15·2	—	1·0
	1902A L.E.	0·9	1·0	0·5	1·0	9·0	—	1·0
4 days	1903A R.E.	3·4	0·6	0·6	—	—	—	—
	1903A L.E.	6·3	0·9	0·6	—	—	—	—
	1909A R.E.	0·1	0·2	0·5	—	—	—	—
	1909A L.E.	0·5	0·2	0·5	—	—	—	—

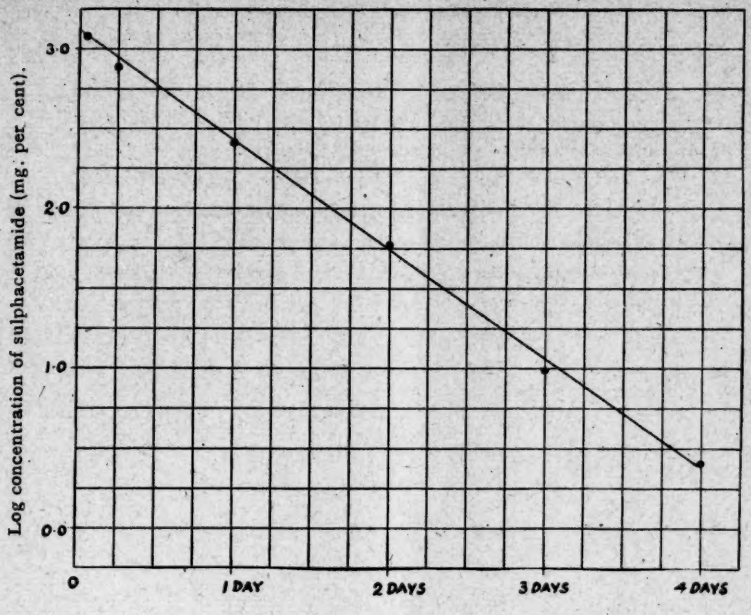

FIG. 2.

Persistence of sulphacetamide in the vitreous following intra-vitreous injection of 30 mg. sodium sulphacetamide.

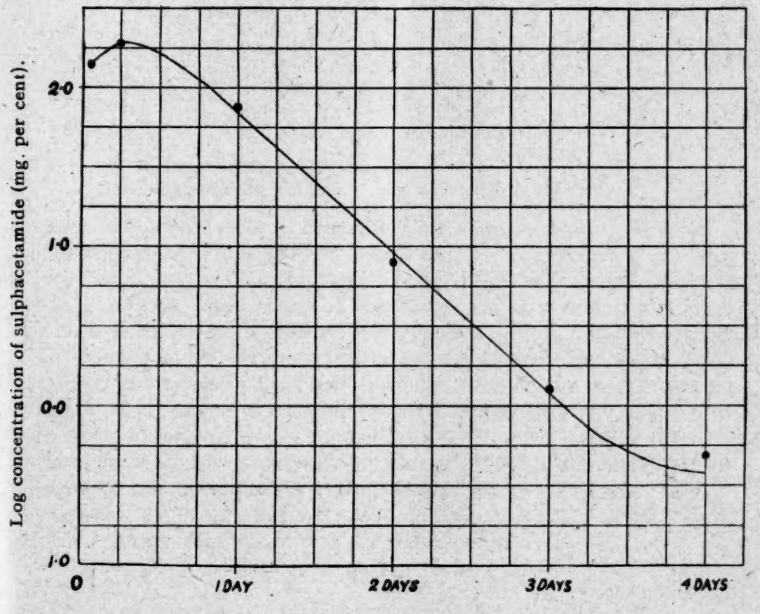

FIG. 3.

Persistence of sulphacetamide in the cornea following intra-vitreous injection of 30 mg. sodium sulphacetamide.

TABLE III

Concentration of penicillin in the aqueous, vitreous and cornea, 1 hour, 6 hours, 1, 2, and 3 days after the intra-vitreous injection of 2000 units of impure sodium penicillin.

Time	Rabbit No.	Concentration of Penicillin (units per ml.)		
		Vitreous	Aqueous	Cornea
1 hour	1892 R.E.	500-1000	20-40	16-32
6 hours	1892 L.E.	500-1000	5-10	8-16
1 day...	1873 R.E.	100-300	—	—
	1873 L.E.	100-300	—	—
	1891 R.E.	100 200	3-6	2-4
	1891 L.E.	200-400	6 12	4-8
	1893 R.E.	200-400	1-2	2-4
	1893 L.E.	200-400	1-2	2-4
2 days	1874 R.E.	6-10	—	—
	1874 L.E.	6-10	—	—
	1890 R.E.	<1/5	<1/10	<1/2
	1890 L.E.	1-2	1/10-1/5	<1/2
	1894 R.E.	5-10	1/10-1/5	<1/4
	1894 L.E.	1-2	1/10	
3 days	1889 R.E.	<1/10	<1/10	<1/2
	1889 L.E.	<1/10	<1/10	<1/2
	1895 R.E.	1/10-1/5	<1/10	<1/4*
	1895 L.E.	1/10-1/5	<1/10	<1/4*

*Tissues from both eyes analysed together.

It was found that penicillin diffused rapidly from the vitreous into the aqueous and cornea which always contained high concentrations within an hour after injection. The concentration of penicillin in the vitreous remained, however, much greater than the concentrations in the aqueous and cornea; the vitreous thus acts as a depot replenishing the drug lost from the other tissues. The concentration of penicillin fell from the high levels at one hour after injection to levels approaching or below the limits of detection after two days in the case of the vitreous. Chemotherapeutic concentrations (i.e., about 1/20th of a unit per ml. and over) were maintained in the vitreous for 2 to 3 days, and in the aqueous and cornea for 1 to 2 days.

TABLE IV

Concentrations of penicillin in the aqueous, vitreous and cornea, 1 hour, 6 hours, 1, 2 and 3 days after intra-vitreous injection of 2000 units of pure sodium penicillin.

Time	Rabbit No.	(Concentration of Penicillin (units per ml.)		
		Vitreous	Aqueous	Cornea
1 hour	1922 R.E.	1000-2000	4-8	4-8
	1922 L.E.	2000-4000	2-4	8-16
	1934 R.E.	500-1000	2-4	1-2
	1934 L.E.	500-1000	2-4	2-4
	1938 R.E.	—	25-50	—
	1938 L.E.	—	—	—
6 hours	1921 R.E.	500-1000	8-16	4-8
	1921 L.E.	1000-2000	2-4	4-8
	1935 R.E.	1000-2000	8-16	8-16
	1935 L.E.	500-1000	8-16	8-16
	1939 R.E.	—	1/2-3	—
	1939 L.E.	—	3-6	—
1 day	1920 R.E.	64-128	<1/4	<1/2
	1920 L.E.	32-64	1/4-1/2	1/2-1
	1936 R.E.	16-32	1/4-1/2	1/2
	1936 L.E.	32-64	1/2-1	1/2-1
	1940 R.E.	—	1/2-1	—
	1940 L.E.	—		—
2 days	1919 R.E.	1/2-1	<1/10	<1/4*
	1919 L.E.	1/2-1	<1/10	
	1937 R.E.	1-2	1/10-1/5	<1/4*
	1937 L.E.	1-2	1/10-1/5	
3 days	1918 R.E.	<1/10	<1/10	<1/4*
	1918 L.E.	<1/10	<1/10	
	1938A R.E.	<1/10	<1/10	<1/4*
	1938A L.E.	<1/10	<1/10	

* Tissues from both eyes analysed together.

In Figs. 4 and 5 the logarithm of the average concentration of penicillin has been plotted against the time after injection. It will be noted that, in the case of pure penicillin, except for a short period immediately after the injection, the logarithm of the

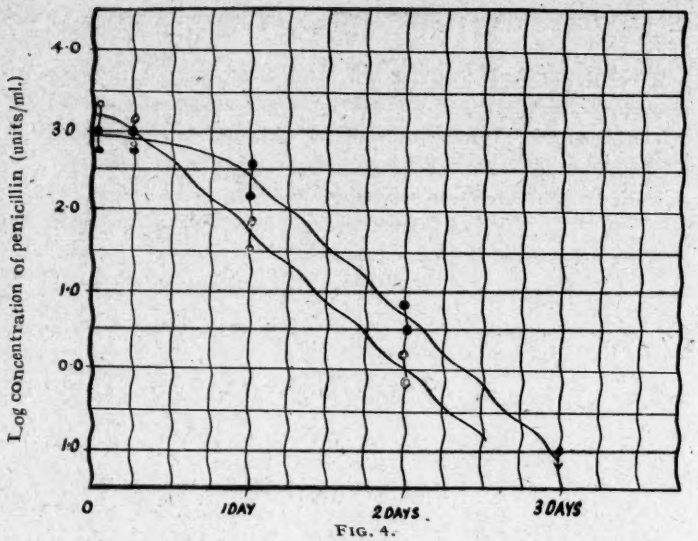

FIG. 4.

Persistence of penicillin in the vitreous following the intra-vitreous injection of 2000 units of penicillin.

● Impure penicillin. O Pure sodium penicillin.

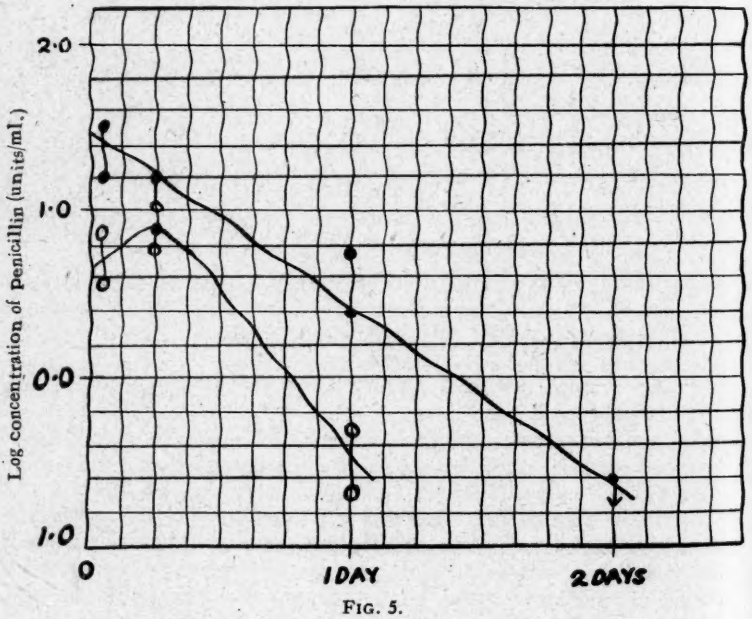

FIG. 5.

Persistence of penicillin in the cornea following the intra-vitreous injection of 2000 units of penicillin.

● Impure penicillin. O Pure sodium penicillin.

concentration diminishes in inverse proportion with the time after injection. In the case of impure penicillin, the fall in concentration is somewhat delayed during the first twenty-four hours.

(c) *Injection of sodium sulphacetamide and sodium penicillin combined into the normal vitreous.* Experiments *in vitro* showed that incubation of sodium penicillin with sodium sulphacetamide for 24 hours at 37°C. did not destroy any appreciable amount of penicillin.

Table V shows the results of experiments in which 0·1 ml. of 30 per cent. sodium sulphacetamide containing 2000 units of pure

TABLE V

Concentrations of penicillin and sulphacetamide in the ocular fluids and tissues after the intra-vitreous injection of 2000 units pure sodium penicillin, and 0·1 ml. 30 per cent. sodium sulphacetamide combined, into normal eyes.

Time	Rabbit No.	Concentration of penicillin (units/ml.)			Concentration of sulphacetamide (mg./100s.)				
		Vitreous	Aqueous	Cornea	Vitreous	Aqueous	Cornea	Iris	Sclera
1 day	1941 R.E.	16-32	½-1*	1	145	43·5	47·8	61·1	17·9
	1941 L.E.	16-32		1-2	165		55·3	75·2	107
2 days	1942 R.E.	<½	<1/10*	<½*	3·9	2·5*	—	—	8·0
	1942 L.E.	½-1			37·7		0·2	0·9	1·8
	1946 R.E.	6-12*	<1/10*	<½*	55·1	2·9*	2·1*	6·4	—
	1946 L.E.				61·4			6·1	—

* Tissue of both eyes analysed together.

sodium penicillin was injected into the vitreous. Except in the case of one rabbit (1942) which was examined at 2 days after injection, when low drug concentrations were found, the results were similar to those obtained when the drugs were injected singly. The combined administration of sulphacetamide and penicillin by intra-vitreous injection does not seem, therefore, to be contra-indicated by any increased rate of disappearance of either drug.

(d) *Injection of sodium sulphacetamide and sodium penicillin into the infected vitreous.* Table VI shows the results of experiments in which the drugs were injected both together and singly into the vitreous of the eyes of rabbits infected by intra-vitreous injection of haemolytic streptococci. Rabbit 1945, at 2 days after injection with penicillin and sulphacetamide combined, showed drug concentrations in the ocular tissues similar to those found in experiments with non-infected eyes. Penicillin alone was injected into the eyes,

TABLE VI

Concentration of penicillin and sulphacetamide in the ocular fluids and tissues after the intra-vitreous injection of 2000 units pure sodium penicillin and 0·1 ml. 30 per cent. sodium sulphacetamide combined, and singly, into infected eyes.

Time	Rabbit No.	Condition	Concentration of penicillin (units per ml.)			Concentration of sulphacetamide (mg/100 g.)			
			Vitreous	Aqueous	Cornea	Vitreous	Aqueous	Cornea	Iris
1 day	1943 R.E.	Infected	½-1	<1/5	<1 perforated	9·3	5·7	2·5	1·9
	1943 L.E.	Infected							
	1951 R.E.	Infected	50-100	1/5-½	1-2 contamin-ated	—	—	—	—
	1951 L.E.	Normal	50-100			—	—	—	—
2 days	1960 R.E.	Infected	—	—	—	56·6	5·4	2·0	8·1
	1960 L.E.	Normal	—	—	—	322	52·3	46·3	62·2
	1945 R.E.	Infected	2-4*	1/10*	<¼*	112	20·7*	19·2*	32·2
	1945 L.E.	Infected				8·2			21·0

* Tissues from both eyes analysed together.

one infected and one normal, of rabbit 1951; after one day the penicillin concentrations in the vitreous fluids of the two eyes were similar. On the other hand, in rabbits 1943 (injected with penicillin and sulphacetamide combined), and 1960 (injected with sulphacetamide alone) the drug concentrations at one day after injection were considerably lower in the infected eyes than in normal eyes. It appears that in some cases of infection, disappearance of the drug from the eye is accelerated, but even so, chemotherapeutic concentrations are maintained for about one day after intra-vitreous injection.

Section III. Effect of Drugs on experimentally produced infections of the Vitreous Body

METHODS

In all animals both eyes were infected, one eye in each animal was treated, while the other served as control and received an injection of saline. Intra-ocular infection was produced, by the injection into the vitreous, of virulent haemolytic streptococci, the strain (1c) being that previously used in the production of corneal lesions (Robson & Scott, 1944); 0·02 c.c. of a broth culture diluted 1:1000 was the standard dose and was followed by the therapeutic agent, after an interval of 1, 6 or 24 hours. In a few experiments a second injection of the drug was given 48 hours later. The dose was always

0·1 c.c. of a 30 per cent. solution, except for penicillin, when the concentration was 20,000 units c.c. At the end of ten days the animals were killed, cultures were taken from the vitreous and some of the eyes were sectioned.

RESULTS

In untreated eyes signs of a severe reaction were evident within 24 hours of inoculation. There was a severe uveitis, shown by exudates into the vitreous and acute iritis. Twenty-four hours later, the whole vitreous was usually opaque and hypopyon was frequently present. At the end of the experiment there was a vitreous abscess in most of these eyes, and in the remainder the vitreous was completely opaque. The effects of treatment are shown in Table VII.

TABLE VII

Showing the effect of various drugs on the development of vitreous infections.

Drug	Number of Animals	Interval between inoculation and treatment	Result treated eyes
		Hours	
Penicillin	3	1	No infection
Penicillin	1	6	No infection
Pure penicillin ...	2	6	No infection
Pure penicillin ...	3	24 and 72	As controls
Sodium sulphacetamide	4	1	No infection
Sodium sulphacetamide	2	1	Infection delayed
Pure penicillin and sodium sulphacetamide	3	24 and 72	As controls
Marfanil	2	1	No infection
Marfanil	2	6	No infection
V.335	2	1	No infection

It will be seen that penicillin prevented the development of infection when injected up to 6 hours after inoculation but had no effect when the treatment was delayed for 24 hours, even if the drug was combined with sodium sulphacetamide.

Sodium sulphacetamide alone injected 1 hour after inoculation prevented development of infection in some of the cases—merely delaying it in others.

Marfanil and V. 335 gave favourable results, but in view of their obvious toxicity to ocular tissues, no further attention was given to them.

The cultures made from the vitreous of the untreated eyes showed growth of haemolytic streptococci in about 50 per cent. of cases but

in the remainder the abscess had apparently become sterile and the cultures were negative. No haemolytic streptococci were recovered from any of the treated eyes.

In a number of the experiments in which the infection had obviously been controlled, certain effects were noted in the vitreous and retina of treated eyes which, in the light of the experiments described in Section I, could, with confidence, be attributed to the toxic effects of the drugs.

Discussion

An attempt has been made to investigate the value and the practicability of injecting drugs intra-vitreously.

Ophthalmologists, understandably, are hesitant to use this method on account of the possible damage to the vitreous gel, the retina, etc. Experimentally, using no surface diathermy, a small needle could be introduced into the vitreous and a small quantity of saline injected without any ill effects. With the exception of pure penicillin, all the drugs introduced into the vitreous, including impure penicillin, were highly damaging to the retina, to a degree which excludes their use clinically. Pure penicillin in some cases was shown to cause small areas of retinal damage—but slight by comparison with impure penicillin or any of the other drugs. Under favourable conditions penicillin introduced by this means is highly effective in the control of infections of the vitreous body, and the diffusion experiments demonstrate that the drug diffuses but slowly from it, so maintaining a chemo-therapeutic concentration for 2-3 days after a single injection, in contrast to its rapid disappearance when injected into most other tissues in the body. In cases in which an eye is seriously endangered by infection in the vitreous it appears justifiable to consider the use of pure penicillin by intra-vitreous injection—the control of the infection more than outweighing the possibility of small areas of retinal damage. If doses comparable to those used in the experiments are given, it would appear sufficient to repeat the injections at intervals of two to three days; the slow diffusion from the vitreous permitting a therapeutic level of the drug to remain for that time.

Summary

The toxic effects and rate of diffusion of certain drugs introduced into the vitreous of rabbits have been investigated.

The therapeutic value of these drugs in experimentally produced vitreous infections is recorded.

Impure penicillin, sodium sulphacetamide, marfanil and V.335 do not appear to have a clinical value by intra-vitreous injection because of the damage they do to the retina.

Pure sodium penicillin sometimes damages the retina slightly when injected intra-vitreously, but its use by this means seems indicated and justifiable in certain cases of infection.

We are very grateful to Dr. W. B. Levinthal for his help in this work and to the W. H. Ross Foundation (Scotland) for the Prevention of Blindness, who defrayed the expenses. The pure penicillin was kindly supplied by Glaxo Laboratories Ltd., the sodium sulphacetamide (Albucid soluble) and marfanil by British Schering Ltd., and the V.335 by the Boots Pure Drug Company Ltd.

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A CASE OF THE LAURENCE-MOON-BIEDL SYNDROME SHOWING ATYPICAL RETINITIS PIGMENTOSA ASSOCIATED WITH MACULAR DYSTROPHY*

BY

CHARLES TAYLOR

LONDON

IN their comprehensive studies on the Laurence-Moon-Biedl syndrome, Cockayne, Krestin and Sorsby (1935), and Sorsby, Avery and Cockayne (1939) have shown that the fundus lesion may be an atypical rather than typical retinitis pigmentosa, and that macular dystrophy with optic atrophy may replace either of these, an observation also made more recently by Lyle (1946). The present case report is of interest in that it shows the combination of atypical retinitis pigmentosa with macular dystrophy. The great rarity of the association of retinitis pigmentosa and macular dystrophy and its hereditary character have been brought out by Sorsby (1940 and 1941).

Case report

Past History. T. S., aged 24 years, was fat at birth. There was some loss of weight following illness at 3 weeks (said to be "threatened with meningitis"). No attempt was made at talking

* Received for publication, January 29, 1947.

until his fifth year when he was sent to school. During his first year at school lenses were prescribed by an ophthalmologist and during his school life he has always occupied the front bench. As far as he can remember there has always been difficulty in getting around after dusk. He rode a bicycle until he was twelve years old, but gave up cycling when he collided with a woman who was crossing the road. In the same year his master forbade him to play cricket. His education was carried on at a private (not "special") school until he was sixteen years of age when it seemed hopeless to continue. He had a variety of posts which he could not retain and

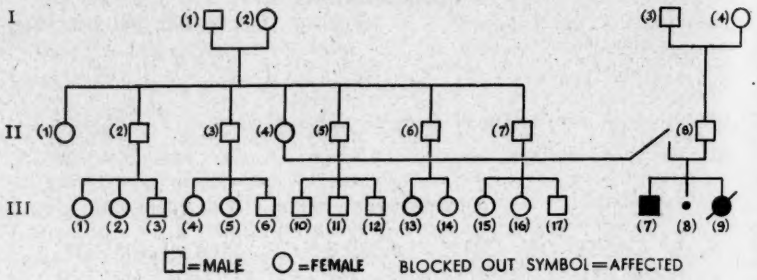

FIG. I. (Three generations only).

II (1) Died in infancy from diphtheria.
(2) Died of sarcoma of spine at 38 years.
(3) (6) (7) Short-sighted.

III (5) Tuberculosis of hip.
(7) Patient (T. S.).
(8) Miscarriage (•).
(9) Still-born, affected.
(14) Died at 3 years from diphtheria; had cleft palate.

is now employed in a factory, where, by pulling a lever pieces are punched out in a sheet of metal to retain hypodermic needles.

Family history. (Fig. 1). His father and mother are not related. They are both English. The father has always enjoyed good health but the mother has had two nervous breakdowns. The Wassermann reaction in both of them was negative. On the father's side of the family a brother and sister of the great grandmother died in infancy, and a great aunt had several miscarriages and two children who died at one year old, one of which was said to have been born blind.

On the mother's side of the family two children of a great aunt died as babies and one great aunt was very fat.

T. S. was the first born. Twice during pregnancy abortion was threatened. A year later there was a four months' miscarriage, but no details of the foetus are available. The third pregnancy resulted in a stillborn female child with extra fingers and toes and "part of the head missing."

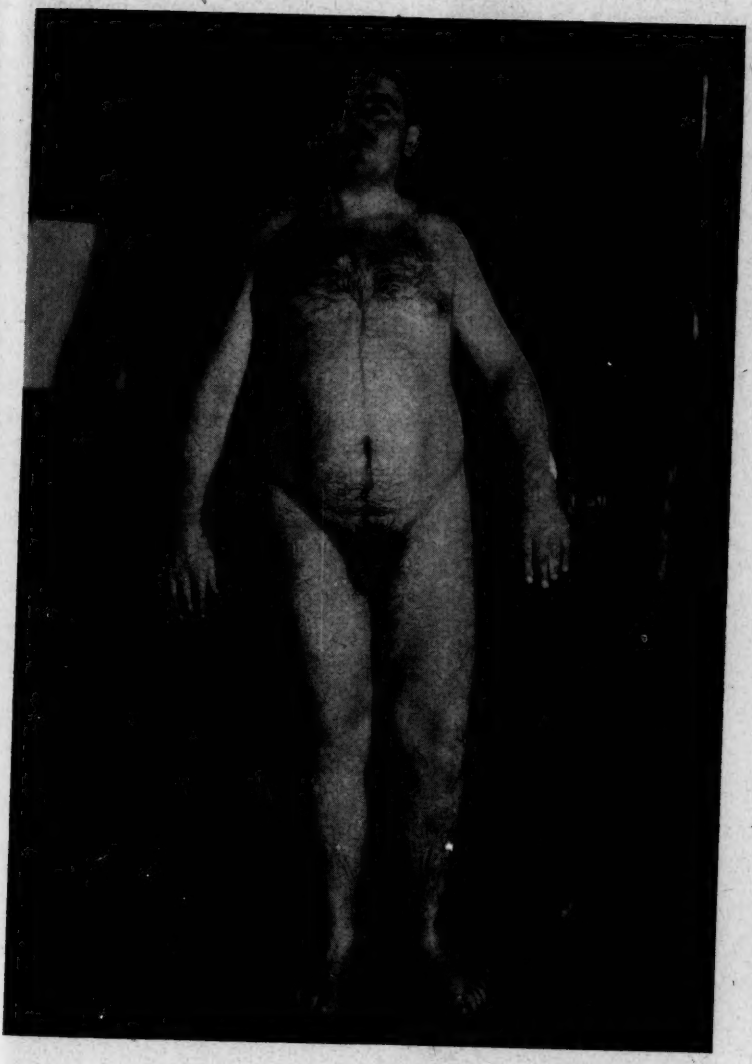

FIG. 2.

Examination. T. S. is placid and co-operative. Mental retardation is present in only a minor degree and in spite of his visual disability he has a fair knowledge of recent events. He is distinctly obese (Fig. 2). His height is 5 ft. 6 in. and his weight 14 st. 2 lb. The fat is distributed chiefly on face, chest, abdomen and thighs. His hair is dark. He presents the male distribution of hair on the body and has to shave every day. The testicles are descended and within normal limits of size. The penis is undersized and the voice high-pitched.

Scars are present on the ulnar side of the right hand over the head of the fifth metacarpal and on the outer side of each foot over the heads of the fifth metatarsals. The extra digits were removed in childhood. Dorsal scoliosis and genu valgum are present.

Vision of each eye with correction:—

$$\left(\text{R.}\ \frac{-1{\cdot}50\text{ D. sph.}}{-2{\cdot}0\text{ D. cyl. }60^\circ}\ \text{L.}\ \frac{-1{\cdot}0\text{ D. sph.}}{-2{\cdot}0\text{ D. cyl. }180^\circ}\right)$$

and without correction is 2/60 after much searching. There is complete and absolute loss of the peripheral fields and as far as can be ascertained only small receptive areas in the perimacular regions remain. The left eye is divergent 5-10 degrees. Both pupils are equal and react to light and convergence accommodation. Constant

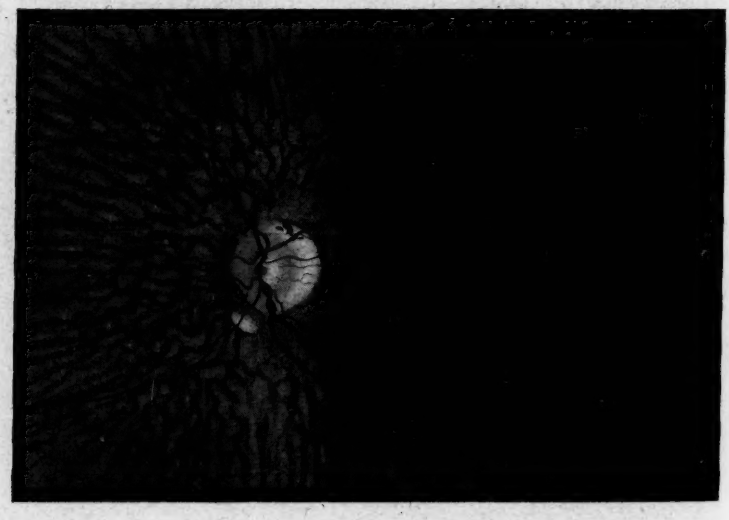

FIG. 3.

Left fundus of T. S.

bilateral nystagmus of the pendulum type is present. It is slow in rate, and increased in range on lateral fixation. A small posterior polar cataract is present in each eye. The fundi (Fig. 3) are lacklustre. Small patches of pigment of varying shapes are scattered over the fundi but "bone corpuscle" pigmentation is not predominant. In addition there is a fine peppering of pigment where the tapeto-retinal atrophy is more marked. Occasional small circumscribed areas of retino-choroidal atrophy are present. The maculae are spotted with pigment. The retinal vessels are diminished in calibre. Unmasking of the choroidal vessels is present over the greater part of both fundi except in the macular and perimacular regions.

Motor and sensory functions of the cranial nerves (apart from 2nd nerves) are normal.

Muscle tone and power in the limbs is good. There is no ataxia. Deep and superficial reflexes are normal and sensation good.

Examination of heart, lungs, and abdomen reveals no abnormality.

Blood pressure: Systolic 128. Diastolic 87. *Urine:* No abnormality. No polyuria or polydipsia. *Blood:* Wassermann reaction: negative. X-ray of skull shows normal conformation. The sella turcica shows no abnormality. X-ray of hands and feet: nil abnormal.

Remarks

Reviews of the collected families present a large number of miscarriages and early deaths indicating that the expression of the genes may be so severe as to result in non-viability or early death. In this sibship it may be that the miscarriage was due to this cause and there is little doubt that this accounts for the still birth of the affected female child.

The present case taken in connection with the previously reported cases, indicates that the range of fundus lesions in the Laurence-Moon-Biedl syndrome extends to at least four variants of tapeto-retinal degeneration: typical retinitis pigmentosa, atypical retinitis pigmentosa, macular dystrophy, and atypical retinitis pigmentosa combined with macular dystrophy.

I am indebted to Mr. L. H. Savin for the opportunity to report the case, and to Professor Arnold Sorsby for his kind assistance.

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THE ACTION OF SULPHANILAMIDE ON RABBITS' LENSES IN VITRO*†

BY

A. BAKKER

GRONINGEN

Introduction

IN a communication published some years ago[1] I described a number of introductory experiments which had the object of showing that the perfusion culture method of de Haan[14] was excellently serviceable for keeping alive rabbits' lenses in vitro for many days. This was the first time that it seemed possible to preserve that extraordinarily vulnerable tissue in such a good condition outside the body. All attempts made in that direction had always miscarried until then[11].

These preliminary experiments convincingly demonstrated the usefulness of this method. Of course good results can only be obtained when the lens is not injured during the operation.

One of the most striking advantages of the perfusion culture method is the *continual* renewal of the nutrient medium. This liquid, obtained from the abdominal cavity of rabbits and in its composition resembling aqueous humour very much, passes the explants in an uninterrupted current. Probably it is for that very reason that I succeeded in obtaining such good results.

The more important facts of my research work, showing evidence of the high vitality of the explanted lenses, may be summarized as follows:—

1. Unaltered metabolism even in explants several days old. The lenses maintain their normal transparency for many weeks.

2. Lenses of young animals show symptoms of growth, apparent from mitotic cell divisions in the equator region.

3. Ascorbic acid can freely diffuse through the capsule in both directions. When the nutrient liquid contains an adequate quantity of this vitamin its concentration in the lens has normal values too[2]. This indicates that the permeability of the capsule of the explanted lenses does not change.

4. Regeneration of experimentally wounded capsules starts and goes on *in vitro* in exactly the same way as *in vivo*. The final result is in both circumstances a newly formed capsule[3].

In subsequent experiments not only the lens but also other ocular tissues, such as the iris, the choroid, the retina and the ciliary body were explanted with equally good results[4]. This enlargement of the

* From the Histological Institute, University Groningen (Director: Professor J. de Haan, M.D.).

† Received for publication, January 7, 1947.

usefulness of our culture method enabled us to investigate the influence of radiant energy on the crystalline lens, covered or not by the iris[5]. The conception of Vogt and co-workers[13] that the lens absorbs the light rays of long wave-lengths in large quantities could be refuted. My experiments showed that the explanted lens only became cataractous under the influence of heat rays, when it was covered by the pigmented iris. Thus my experiments agreed fully with those of Goldmann[13]. Although Goldmann and I worked along quite different lines, we both came to the conclusion that the lens is *indirectly* burnt by the heat rays absorbed in the pigmented iris.

This short enumeration of the results obtained with the explanted rabbits' lenses may give an impression of the possibilities of this culture method.

Subsequently I carried out further investigations with the object of determining whether this method could be made subservient to testing drugs on their toxicity. I chose sulphanilamide (prontosil album), as this drug is easily soluble in water and as it was used in our laboratory to fight against probable infections of the nutrient liquid.

There was still another reason to investigate the influence of sulphanilamide on the lens, as it is known that this drug inhibits the enzyme action of carbonic anhydrase. This enzyme (discovered by Brinkman and Margaria[12]) catalyzes the reaction $H_2CO_3 \rightleftarrows CO_2 + H_2O$. Now the lens contains a very high concentration of this enzyme and as I could show[6] that in cataractous lenses the concentration of carbonic anhydrase decreases considerably, it is probable that an intimate relation exists between this enzyme and the transparency of the lens. In other words the behaviour of the explanted lens under the influence of sulphanilamide can enable us to get an impression of the toxic action of this drug.

A simple method to determine the concentration of carbonic anhydrase in lenses (and in other ocular tissues) is described in a preceding article[7]. Two later papers deal with some activators and inhibitors of this enzyme[8, 9].

For the details of this culture method and the technique I must refer to my former publications.

At the end of each experiment the enzyme concentration and the content of sulphanilamide in the lenses is determined. Sometimes the lens is microscopically examined, this, however, does not yield any important data.

Experimental results

Introductory experiments taught us that a concentration of 5 mgr. per cent. of sulphanilamide in the nutrient fluid (a concentration lower than the blood concentration in the usual therapeutic dose)

was quite harmless for lenses of adult rabbits. In eight day old explants the lenses did not show any opacities (perfusion velocity of the nutrient fluid 1 drop in about 50 to 60 seconds).

A content of 20 mgr. per cent. of sulphanilamide was not noxious to lenses of a seven week old rabbit. After a stay of three days in the culture vessel the lenses were still quite clear.

When, however, the concentration was raised to 400 mgr. per cent. the lenses of a four week old rabbit got very opaque in the short time of two hours. After 15 hours transparency was so much impaired that letters on an underlying paper could no longer be read. After three days the culture was stopped. The opacities were especially localized in the posterior cortex, but also the anterior cortex showed some of them. The lenses contained 385 mgr. per cent. of sulphanilamide, demonstrating that the capsule is freely permeable to this drug. The enzyme action was reduced to 1/5 of its original value.

Though the deleterious influence to lenses of very young animals was evident, the toxicity of sulphanilamide for lenses of adult rabbits was less pronounced. It was not until after five days that lenses of the latter in the same concentration (400 mgr. per cent.) showed some opacities. After eight days the enzyme action in these lenses was reduced to less than 1/6 of its original value.

Conclusions

The perfusion culture method proved to be able to give reliable information on the toxic action of chemicals. With the aid of the same method too, I was formerly able to give an affirmative answer to the question whether galactose has a *direct* noxious influence on the lens[10].

The present experiments have shown that sulphanilamide has not any injurious effect on rabbits' lenses when the concentration is not raised above the level reached in normal therapeutic doses. Yet, some caution is advisable in using this drug. Mrs. Schappert-Kimmijser told me (verbal communication) that in a 43 year old patient, suffering from erysipelas faciei and treated with prontosil for no less than 4 months, cataractous changes in both lenses of capsular and sub-capsular character developed.

There was a striking difference between the behaviour of young and old lenses in my experiments. The younger the animals were the more their lenses were susceptible to the noxious influence of sulphanilamide

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A CASE OF CONGENITAL VERTICAL SHORTNESS OF THE LIDS COMBINED WITH TETRASTICHIASIS*

BY

DR. J. LANDAU

(From the Eye Department of the Hadassah University Hospital, Jerusalem, Director : Professor A. Feigenbaum).

CONGENITAL shortness of the lids was entensively studied by E. Fuchs[1 2] in 1885. Congenital absence (ablepharon) or maximal shortness (microblepharon) of the lids has been observed repeatedly, partly in monsters, and also in otherwise normal individuals (*cf.* Manz, *Handbuch. d. Ophthal., Graefe-Saemisch.*, Vol. II, p. 103). Stellwag described mainly the smallness of the lids in the horizontal diameter and the ensuing shortness of the palpebral fissure in this direction but not what, in the opinion of the writer, should be called vertical shortness of the lids. It was left to Fuchs to coin the expressions "height of the lid" and "vertical extension of the skin of the lid". "Height of the lid" is the maximum distance between the lid margin and the centre (*i.e.* half the breadth) of the eyebrow. In measuring this height the individual is asked to close the eyes

* Received for publication, December 20, 1946.

lightly as though he were sleeping. "Vertical extension of the lids" is the maximal distance measured between the free lid margin and the centre of the eyebrow while the lid is held by the cilia and maximally stretched. These two measurements can be obtained only for the upper lid as there is no fixed demarcation between the lower lid and the skin of the cheek and no reference point exists for measuring the lower lid. The proportion between height and vertical extension of the lid is the co-efficient. Once this co-efficient falls below a certain value (1·5) the lid closure becomes abnormal: Normal closure of the lids is possible only if the height of the stretched upper lid is greater by at least one half than the height in a lightly closed state. The co-efficient varies from 1·5 in infants to 1·9 in old people. When the lid closure is not complete, lagophthalmos results. Complications of this condition are conjunctivitis and blepharitis (usually ulcerative). The cornea is rarely involved.

Von Herrenschwand[3] published a case of congenital (vertical) shortness of the lids with ectropion of the palpebral conjunctiva. The lid margins were covered with conjunctiva, there were only a few eyelashes present and the lacrymal puncta were absent. The tarsi were normal.

Urmetzer[4] presented a case of abnormal (vertical) shortness of the lids with marked hyperaemia of the lid margins, madarosis and a slight ectropion of the lower lid. Complete closure of the lids was impossible and the stretched lids were hardly longer than the relaxed ones.

The following case was observed at our out-patient department.

L. J., a boy aged 16 years, showed with closed lids a lagophthalmos of about 2·5 millimetres in both eyes (Fig. 1). The height of the

FIG. 1.

lids was 24 millimetres, the vertical extension 30 millimetres. The co-efficient was, therefore, 1·24. In both upper lids the cutaneous part of the lid margin was slightly everted, particularly in the temporal portion (Fig. 2). There were in both upper lids four rows

FIG. 2.

FIG. 3.

of equally well developed eyelashes. In the palpebral conjunctiva of both upper lids a fine dark line was visible in the subtarsal sulcus from which thin vertical streaks were extending (Fig. 3).

Visual Acuity: R.E. + 0·5 D. sph. c. + 0·5 D. cyl. 180° 5/5 (partly); L.E. + 0·5 D. sph. c. + 0·5 D. cyl. 180° 5/5 (partly).

There was no irritation of the lid margins or the conjunctiva. Apart from an acute blepharo-conjunctivitis in 1939, and a stye in 1941 no inflammatory conditions of the lids had occurred until now.

Discussion

To explain congenital distichiasis Kuhnt[5] assumes a heterologous developmental anomaly. Cilia develop instead of Meibomian glands not only at the anterior but also at the posterior edge of the lid margin, owing to an abnormal preformation of unknown origin. Brailey[6] is also of the opinion that the epithelial invagination of the material destined to form the Meibomian glands failed to take place and that eyelashes developed in their stead, corresponding exactly to the ducts of the glands. Erdmann[7] conversely, considers the glands which belong to the posterior row of cilia as a formation of

cilia and Meibomian glands from the same *anlage*, differentiation having failed to take place owing to an unknown cause. According to him the epithelial cone constituting the first *anlage* of both organs may develop into either an eyelash or an acinus of a Meibomian gland. An increase in the number of cilia, polytrichiasis or hypertrichosis, may be congenital or acquired. In congenital polytrichiasis the cilia are arranged in two or even three or four rows instead of only one, conditions which are called distichiasis, tristichiasis or tetrastichiasis[8]. Fuchs[9] reserves the term distichiasis for those rare cases where there are congenitally two regular rows of cilia in an otherwise normally developed, not inflamed lid. Aubaret[10] also considers congenital distichiasis to be a rare anomaly.

The case presented above shows in addition to congenital vertical shortness of the lids, the rare picture of tetrastichiasis. The dark lines visible in the sulcus subtarsalis seem to be the hair follicles of the supernumerary cilia which have developed instead of the Meibomian glands. In spite of the existing shortness of the lids and the resulting lagophthalmos, the lid margins are altogether free from irritation, possibly because the cilia are regular and well developed. According to Schreiber[8] the case of congenital symmetrical shortness of the lids with congenital symmetrical ectropion of the lid conjunctiva described by von Herrenschwand[3] is unique in the literature. In the present case the partial eversion of the upper lid represents an abortive form of this condition.

While almost all cases of the Fuchs[1 2] showed inflammatory changes of the conjunctiva and the lid margins, in the case described here there were no signs of irritation. The cases of von Herrenschwand[3] and Urmetzer[4] had scanty cilia or no cilia at all (madarosis), whereas in our case there were four rows of regular, healthy cilia. According to the table of Fuchs[2] the normal co-efficient for the age of 16 years is 1·6 while in our case it is 1·24.

Summary

1. A case of congenital shortness of the lids in the vertical direction ("vertical shortness"), combined with tetrastichiasis, is presented.

2. A partial eversion of the cutaneous part of the upper lid margin was observed.

3. In spite of the existing lagophthalmos the eyes remained free from irritation or inflammation, possibly because of the co-existing hypertrichosis.

4. In the sulcus subtarsalis a dark line was apparent due to the hair follicles of the supernumerary cilia showing through the conjunctiva. These have probably taken the place of the Meibomian glands occupying their ducts.

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RESEARCH IN ZURICH

"Summary of the work on the pathological changes in the aqueous-humour and the blood-aqueous barrier, at Zurich."*

BY

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THE research at present being carried out at the University Augenklinik at Zurich is devoted to the study of the aqueous humour and the blood-aqueous barrier.

This work was started by Professor Marc Amsler and his associates in Lausanne in 1940, and was mainly concerned with the albumen and cell-content of the aqueous in disease of the anterior segment. Since the Professor's appointment as Director the work has been continued and augmented at this clinic.

The aqueous humour

The specimen of aqueous humour is obtained in the following way:—A smear and culture are taken from the conjunctival sac. The lids are then held open by a speculum, and a small scraping of corneal epithelium is taken from the lower and outer part of the cornea about three millimetres from the limbus. This area is painted with 5 per cent. iodine solution. The eye is now fixed by an assistant, and a puncture made through the painted area in a plane parallel to the iris. This puncture is made with a special needle devised by Professor Amsler which is placed on a 1 c.c. (tuberculin) syringe.

* Received for publication, January 29, 1947.

The aqueous is then slowly withdrawn, and the needle removed in the same plane as that of its insertion.

This relatively simple procedure can easily be performed in the out-patient department.

The following investigations are made on the specimens obtained.

The conjunctival smear is examined after staining, and the state of the cells noted. The result of the conjunctival culture is correlated with the findings in the culture of the aqueous. The cell scraping of the corneal epithelium is also examined microscopically. A drop of the aqueous is used in the Pandy reaction (this reaction for the quantitative detection of albumen being selected for its reasonably accurate clinical results on small specimens). Another drop is placed in a counting cell (Fuchs-Rosenthal) to give a true figure of the cells/mm^3. A culture is taken in a broth medium (Rosenow). The remaining fluid is placed in a capillary centrifuge tube in which the centrifuged matter is deposited on a cover-glass; this specimen is stained with the May-Grunwald and Giemsa reagents and mounted, the slide is then examined to ascertain the type of cell present. If there is sufficient fluid a specimen is also stained by Gram's method.

All this has to be carried out on one-fifth of a c.c. of fluid or less, and the apparatus used is adapted for these minute quantities.

These examinations were controlled by an investigation of 300 normal eyes.

Serum reactions were carried out on a few cases early in the series, but were given up on account of the greater need for the fluid in other investigations. It was found that the W.R. in the aqueous is never positive if the blood reaction is negative, and even with a positive blood reaction unless there is albumen present the result is negative.

So far just over 1900 a.c. punctures have been performed in the course of this research.

Findings

1. In accord with other authors who have studied this question, it has been found that the normal aqueous contains between 0 and 1 cell/mm^3.

2. In anterior uveitis and deep ulcers of the cornea, the number of cells is increased in varying proportions. The figures most often obtained vary between 30 and 200 cells/mm^3. A few cases rise even to 100,000 cells/mm^3.

3. In acute inflammations, the albumens are increased in proportion to the number of cells.

4. In chronic inflammations and other diseases it has been found constantly that there is a dissociation between the albumens and the cells, comparable to that observed in the pathology of the cerebro-spinal fluid.

5. The researches on the morphology and origin of the cells has proved that they are derived from the blood and the neighbouring tissues. The predominant rôle of the reticulo-endothelial system in a great number of cases of chronic irido-cyclitis has been noticed.

6. The phagocytic and antitoxic function of the cells desquamated into the anterior chamber has been indicated by the presence of micro- and macrophages in the specimens.

7. Out of 651 cases of exogenous and endogenous irido-cyclitis, keratitis and panophthalmitis, 19 per cent. showed large reticulo-endothelial cells which had phagocytosed micro-organisms. Those that were most commonly seen were cocci with variable morphology and staining—thought to be staphylococci in most cases. In perforating wounds one may find Morax-Axenfeld bacilli and pseudo-diphtheroids. Tubercle bacilli have never been found, except in one unusual case in which a positive culture was obtained.

Cultures are very rarely positive (about 3 per cent.) even with strongly positive smears. Altogether the cultures have consisted of

7 Staph. albus.	1 Tubercle bacillus
1 Staph. aureus.	1 Morax-Axenfeld bacillus.
3 Pneumococcus.	6 Pseudo-diphtheroids and
1 Streptococcus.	other unidentified organisms.

8. The presence of micro-organisms in the anterior chamber in the course of keratitis and anterior uveitis throws a light on the aetiology in many cases.

9. The absence of tubercle bacilli in the numerous specimens studied causes doubt as to the preponderant rôle which is attributed to them in the pathogenesis of chronic uveitis, especially as other microbes have been found.

10. The phagocytosed micro-organisms which have been found have indicated the possibility of focal infection, and in many cases a focus has been found suggesting a strong aetiological factor.

The blood-aqueous barrier

Following the work of Ehrlich in 1881 on the use of intra-venous fluorescein (when he noticed that the dye found its way into the anterior chamber); this method has been adapted to the needs of the research here on the permeability of the blood-aqueous wall.

The flourescein is injected intra-venously and relative measurements of its concentration are taken at suitable time intervals during the next 30 minutes.

This is done by means of an adapted slit-lamp in which the illumination of the anterior chamber can be reduced by a resistance while the eye is kept under observation, until the green colouration of the aqueous is no longer detectable. Readings are then taken from an amperemeter in the slit-lamp circuit.

These readings are plotted on a chart in graph form; time/amps resistance over a period of half an hour.

A preliminary investigation was carried out on 200 normals. These were carefully selected from individuals in which there was no evidence of ocular or general disease.

The results in these cases show that:—

1. There is a normal excretion of the dye into the anterior chamber. The analysis of the 200 cases shows that there is a regular and gradual rise of fluorescein concentration during the time of examination.

2. The permeability curves of the two normal eyes of an individual are the same.

3. The day to day variations in a normal eye are well within the limits of the normal band.

4. The normal for children up to about 15-17 years, is a little higher than the normal band for adults.

This research was then directed to the study of the altered permeability in disease, at first only in ocular disease, but more recently in cases with general diseases.

More than 1,000 patients have been examined in this way. The pathological curves of increased permeability are situated above the normal band and are characterised by an immediate rapid rise of concentration to a point where the concentration remains almost unaltered.

The findings in disease are as follows:—

1. Irido-cyclitis. All degrees of permeability increase, from the slightest forms to the most severe are seen, corresponding to the severity of the irido-cyclitis. There is a possibility of early diagnosis in cases where no other sign is visible. A control can be made of therapeutic effect on the permeability.

2. Glaucoma simplex. Some cases show normal or slightly increased permeability, while others show a considerable rise in permeability. It is possible that these alterations in the findings show a differentiation between true simple glaucoma and those tending to an inflammatory aetiology (on these points one's treatment may be altered).

3. Traumata. Contusion and perforating injuries produce a great increase of permeability. It can be seen in cases of unilateral injury, that there is a bilateral rise of permeability although the uninjured eye shows a less marked increase.

4. Other ocular affections causing an increased permeability. As examples: central venous thrombosis, periphlebitis, retinal detachment, choroiditis.

5. General diseases showing an increased permeability (with no sign of ocular inflammation). Bronchial asthma, gastric ulcer, generalised oedema, chronic nephritis, epidemic hepatitis, rheumatic

polyarthritis, obesity, and above all diabetes (40 per cent.), and malignant hypertension. In purpura there is some parallelism between increased permeability and the Rumpel-Leed phenomenon.

6. Pharmacological effects. The pharmacological effects of some drugs commonly used in eye treatment, or which are known to have an effect on the capillary permeability in other parts of the body, have been studied. It has been found that pilocarpine increases the permeability, atropine and homatropine have no effect, adrenalin and l-glaucosan diminish the permeability. Sub-conjunctival injections of slightly hypertonic sodium chloride increase the permeability, calcium injected intra-venously in a dose of 10 c.c. of a 20 per cent. solution in many cases has a diminishing effect. Sub-cutaneous histamine in small doses has an enormously increasing effect.

The Tyndall effect

Since this work was taken up at Zurich, further aspects have been enquired into.

The beam of light from a slit-lamp passing through a proteinaceous aqueous in the anterior chamber shows itself in a flare described by Tyndall in 1869, and called the Tyndall effect.

This can be used as a clinical sign in diagnosis and prognosis of infections of the anterior segment. The Tyndall effect is more marked–the higher the protein content of the aqueous and this is measured by a Tyndall photometer. This also is a modified slit-lamp in which part of the illumination is reflected through a pair of crossed polarising filters to the microscope. On looking through the eye-piece one sees an oblong strip of light the brightness of which can be adjusted by rotation of one of the filters.

The image of the slit-lamp beam passing through the aqueous is seen immediately above the polarised image. The latter is adjusted until the appearance of both images is identical, and an average of four readings taken.

The results can be plotted on a graph (the Tyndall Nephelogram) giving an accurate record of the variations of the phenomenon.

When plotted against time the graph will show a rise and fall which corresponds closely to the clinical deterioration and improvement, the more useful because of the early appearance of this sign in disease of the anterior segment.

In comparing the uses of the Tyndall effect with that of the fluorescein permeability, we see that the Tyndall effect shows the permeability of the damaged blood-aqueous barrier to proteins and large molecules; while the fluorescein permeability shows the more minute changes in the permeability of the wall to smaller particles. Secondly, whereas the normal barrier will not allow a positive

Tyndall effect, it will allow fluorescein to pass through. Thus the fluorescein will give an earlier and more sensitive impression.

The most recent trends here are aimed at finding out the effect of pathological aqueous on a tissue culture of fibrocytes. It is suspected from clinical observations that the pathological humour will have a detrimental effect on these cells. The work has only just commenced (November, 1946) and no results are available yet.

The aqueous is now also being examined under the ultramicroscope to study the cells, bacteria, and the number and size of the protein particles.

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A GRÖNBLAD-STRANDBERG SYNDROME*

BY

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ANGIOID streaks are a rare form of retinal degeneration and are recognisable by a network of streaks varying in colour from reddish to dark brown. The two components of the syndrome, that is, angioid streaks and pseudo-xanthoma elasticum could be clearly seen in our case. It is suggested that in this disease there is a degeneration of the elastic tissues throughout the body.

* Received for publication, January 18, 1947.

Case Report

Hüseyin K., a worker aged 35 years, complained of blindness in the right eye and was admitted to hospital. He had never before noticed anything strange about his eyes. Personal and past history had no bearing on the case. We questioned him carefully but could not find any trace of a similar eye disease in any relative. Urine analyses showed nothing pathological, arterial blood pressure 70/100 m.m., red and white B.C. number, blood picture and internal organs were normal. Radiological examination of the lungs revealed nothing pathological. Mantoux test and Wassermann reaction were negative, blood cholesterin normal. Externally both eyes were normal. In the right eye central vision was lost, and in the fundus there was a second network behind the retinal vessels, resembling the latter (Fig. 1). Round the papilla was a black, irregular ring from which started many irregular streaks, with ragged borders and of varying width. The streaks were behind the retinal vessels and in front of

RIGHT

FIG. 1.

the choroidal ones. The fundus picture did not reveal whether they belonged to the retina or choroid. Although the streaks usually ended before reaching the peripheral parts of the fundus, some could be seen to meet it. There was a large yellow lesion in the fundus, extending 1 mm. into the vitreous, filling the macular area and reaching the papilla. The lower part of the lesion was surrounded

LEFT

FIG. 2.

by a deep retinal haemorrhage. Near a small artery was a second small haemorrhage, temporal to the macular region. Since the patient had no central vision in the right eye, we obtained its visual field by the Schlosser method. A large central scotoma was revealed (Fig. 3). The left fundus was also abnormal with pigmented streaks as in the right eye, starting from the peripapillary ring and leading to the peripheral parts of the fundus. There were more streaks than in the right eye (Fig. 2). There were three choroidal atrophic patches round the papilla. No macular lesion was present, vision

was 20/25 and visual field normal (Fig. 4). Only macular lesions interfere with vision. Pigmented lines do not apparently affect it.

In 1889 Doyne described the characteristic appearance of the fundus as a network similar to the vessels. Three years later the disease was observed by Plange, Stephenson and Knapp, and named angioid streaks as a clinical entity. The aetiology of the disease is

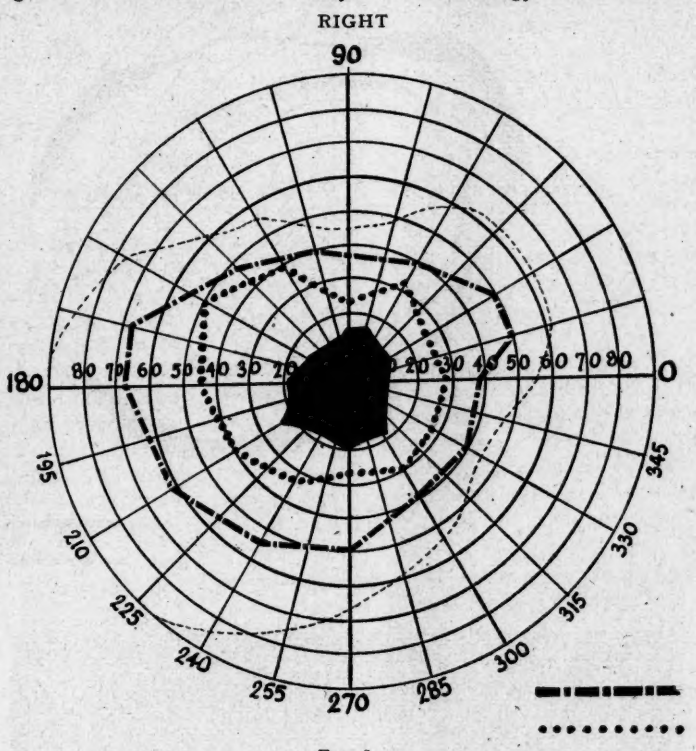

FIG. 3.

not well known. Doyne and Plange suggested that the streaks were haemorrhagic in origin and this was elaborated by Collins. He believed that the haemorrhage was intra-choroidal and that haematogenous pigment was deposited in the perivascular spaces.

The formation of supernumerary new vessels was suggested by Lister and others. Both theories were nevertheless found unsatisfactory.

The deformation of the inner tissues of the eye, particularly of the pigment epithelium, was suggested by Walser, Alt, Coppez, and Danis, the folding being probably produced by some exudative

LEFT

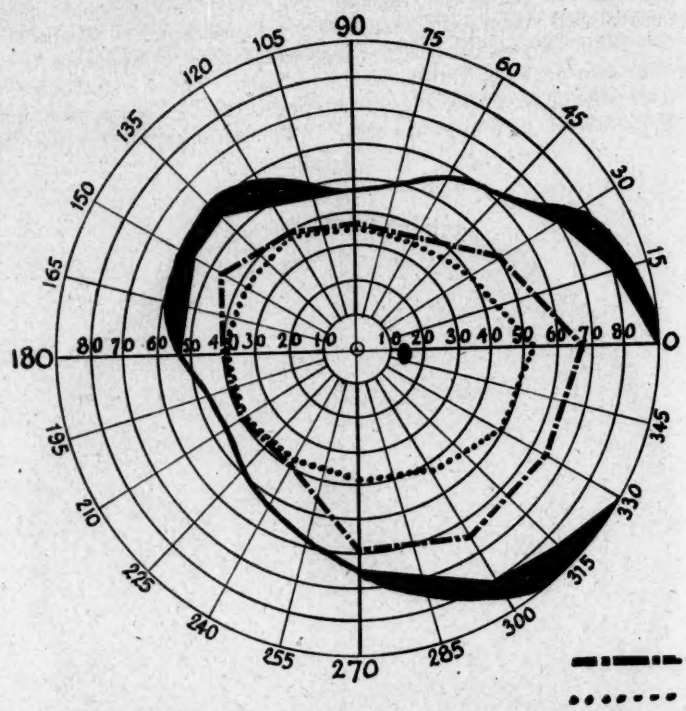

FIG. 4.

FIG. 5.

process in the choroid. Affection of the retina itself by the accumulation under it of pigmentary debris is more fully authenticated by Law's histological findings. This theory, however, was also unsatisfactory.

Deterioration of the elastic elements of Bruch's membrane leading to the formation of fissures was suggested as the aetiological factor by Kofler and Lohmann. The theory attracted little attention, however, until the association of angioid streaks with pseudo-xanthoma elasticum was pointed out by Grönblad.

Our conclusions are in accordance with the last theory. It is a most uncommon disease of obscure aetiology, affecting the elastic tissues throughout the body.

The skin lesions, pointed out by Grönblad, have the appearance of buff or yellow patches situated on the neck, abdomen, flexures and chest. The first two manifestations were apparent in the above-mentioned case. The presence of two conditions together was later observed in many cases. Statistics of Grönblad revealed the fact that 57 out 67 cases skin and fundus appearances together. The association of two lesions was given the name of Grönblad-Strandberg syndrome.

Angioid streaks are caused by the widespread degeneration of the elastic tissues, and can be observed in the posterior pole and in the lamina vitrea. In the elastic structure of the lamina vitrea and in the inner layers of the choroid one may observe some degenerate patches. These patches appear to be due to the reduced resilience of the elastic tissue and may result in fissures and lines. In our case extensive parts of the skin of the neck and the abdomen had a

FIG. 6.

FIG. 7.

parchment-like appearance, and raised yellow streaks and patches could be clearly seen (Figs. 5-6). Although trauma has been quoted as an aetiological factor, no trauma could be noticed in this case.

Pathological examinations were made of the skin of the abdomen:— "A slight hyperkeratosis may be observed in some parts, and an increase in pigmentation in others. In comparison the epidermis has become thinner, and shows accumulations of large protoplasmic vacuolar cells. The collagen fibres have been broken and diminished in size. Scattered infiltrations of inflammatory cells appear in some parts. "Anatomico-Pathological Laboratory, Gülhane Hospital (Fig. 7).

The above findings confirm the degeneration of the elastic elements of skin. Our case, having characteristic ophthalmoscopic and skin lesions, is a typical example of the so-called Grönblad-Strandberg syndrome.

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AN IMPROVED DARK-ADAPTOMETER*

BY

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SOME time ago an instrument was described in this Journal intended for testing dark-adaptation in normal and sub-normal patients. However, when it was tried to investigate gross disturbances (*e.g.*, retinitis pigmentosa), the need was felt for a wider range of readings. When re-designing the apparatus provisions were also made to change the colour of the test-light if desired in order to make the instrument more versatile.

As the general outlay of the apparatus has remained the same except for two relevant items, the reader is referred to the previous paper. In the former design (see previous paper, p. 236, drawing I, "9") a blue glass plate was inserted into the path of rays; as this glass plate could not be easily removed, the light of the stimulus was unvarying blue. The same drawing also showed (see "11") how the intensity of the test-light was being reduced by openings of different size drilled into a metal-strip. A limit of this method was given by the fact that a very fine hole is rather difficult to drill, to keep clean, and to center.

In the present design the aforementioned limitations have been overcome as follows:

(*a*) ***Changing the colour of light:*** A double-walled, rotating disc (see 9A in this paper) replaces the blue filter (9) of the former design. This disc is similar to that used in ophthalmoscopes for changing lenses, and has six openings. Into five of them filters of different colour can be inserted; the sixth hole remains empty, thus passing uncoloured light when brought into position. In the photo the empty opening (6) is shown centered.

(*b*) ***Altering the intensity of light:*** A disc (see 11A in this paper), similar to the colour-filter disc (9A) takes the place of the metal strip (11) used in the previous design. The six openings in this disc are all of equal size and accomodate six grey filters of different transmission. These neutral screens may be obtained from Messrs. Ilford but if less accuracy is needed they can be prepared quite easily by exposing and developing photographic film. Their density* is determined by photometry. As very dark screens can be tested only with

* Received for publication, February 6, 1947.

* Density means $\log_{10}\left(\frac{I_0}{I}\right)$, where I_0 stands for incident light and I for transmitted light; thus a filter transmitting 10 per cent. of the full (100 per cent.) incident light has a density of: log 100 — log 10, or: 2 — 1 = 1.

difficulty, several more transparent neutral filters can be combined as to give the required density. As done for the disc carrying the coloured filters, the openings are marked from "1" to "6". In the photo grey screen number three (with a density of 0·40) has been brought into position. The full range of densities is shown in table I:

TABLE I

Number of opening:	"1"	"2"	"3"	"4"	"5"	"6"
Density:	2·48	1·49	0·40	5·78	4·63	3·60

In order to determine the relative densities of our screens, one of them, e.g. "1" is assumed to be zero. Thus the density of screen two becomes: $1{\cdot}49 - 2{\cdot}48 = -0{\cdot}99$, the density of screen three: $0{\cdot}40 - 2{\cdot}48 = -2{\cdot}08$ etc. Table II lists these values:

TABLE II

Number of opening:	"1"	"2"	"3"	"4"	"5"	"6"
Density — 2·48:	0	—0·99	—2·08	+3·30	+2·15	+1·12

The calibration proper is performed without colour filter, but with grey screen one in position; a light-source calibrated by the National Physical Laboratory, Teddington, serves as a standard. By stopping down the diaphragm of the standard and of the adaptometer simultaneously, a calibration curve is obtained. Though these figures could be directly entered on the cardboard attached to the face of our shutter, it is more convenient to make a correction for blue light, as this colour is preferably used in dark adaptation tests. In the uncoloured light of our lamp the blue filter itself has a density of 2·37; thus 2·37 has to be deducted from the values obtained in the calibration chart. The corrected figures are now entered on the cardboard. The scale (as shown in the photo) reads directly logarithmic units of millimicrolamberts for blue light, if grey screen one is in position. Shifting over to grey screen two which is by 0·99 units more transparent (see Table II) means *adding* 0·99 to the reading of the diaphragm scale. Similarly, as grey screen six is by 1·12 units more opaque than screen one, it calls for a deduction of 1·12. Using white light instead of blue light, 2·37 has to be added (see above).

It will, however, be noticed that no arithmetic at all is involved when testing final thresholds in normal or slightly subnormal cases if blue light is used. For screen one (relative density zero) does not call for a correction. The neighbouring screen (two) which covers most of the sub-normal cases needs simply adding one (or more exactly 0·99).

Thus the threshold shown in the photo has to be read off as: 1·9 (indicated on the scale of the diaphragm), plus 2·37 ("6" on the colour-filter disc indicating white light), plus 2·08 (due to grey screen "3"), the total value being 6·35 log units of millimicrolamberts.

Summary

A dark-adaptometer is described which covers a wide range of intensities of light stimuli and allows the use of different colours.

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CIRCULATORY STUDIES OF THE FUNDUS OF THE EYE*

BY

P. WEINSTEIN *and* J. FORGÁCS

BUDAPEST

OUR investigations assumed first that the difference of pressure between the arterial and venous parts of the capillary system acts as circulatory motor, further, that spontaneous venous pulsation of the fundus of the eye is a sign of a pressure prevailing within the central retinal vein lower than the intra-ocular tension. One hundred cases were examined: fifty of them showing spontaneous pulsation, the other fifty without such. Hardly any difference concerning number of hypertonics and hypotonics, ocular tension, age, sex and brachial blood-pressure could be distinguished between the two groups in question (*see* Table). With those cases in which no

TABLE I

	Pulsating cases 50	Non-pulsating cases 50
Hypertonia	15	15
Hypotonia	7	6
Ocular tension	15-26	13-23
Age	16-79	16-76
Sex	25-25 ♂ ♀	31-19 ♂ ♀
Blood-pressure	164/92	160/90
Appearance of arterial pulsation (mm. mercury suction)	97	141
Appearance of venous pulsation (mm. mercury suction)	27	59
Complication:		
Retinal haemorrhage	2	6
Chorio-retinitis	2	4
Papilloedema	1	2
Atrophy of the optic nerve	1	—
Total	6 (12 per cent.)	12 (24 per cent.)

spontaneous venous pulsation was present, such was elicited by applying Kukan's ophthalmo-dynamometer. We did not transpose the mercury millimetre values at the moment pulsation becomes visible, into values of retinal blood pressure, but in the table only

* Received for publication, January 13, 1947.

that mercury millimetre value of suction is represented, at which venous or arterial pulsation becomes first evident.

The difference of the two groups manifests itself in two directions the drop from arterial and venous diastolic pressure established at a higher level with the non-pulsating cases, than with the pulsating ones (*see* Fig. I), although the value is the same, respectively the difference between arterial and venous pressure is essentially larger with the pulsating eye, The following has to be considered in

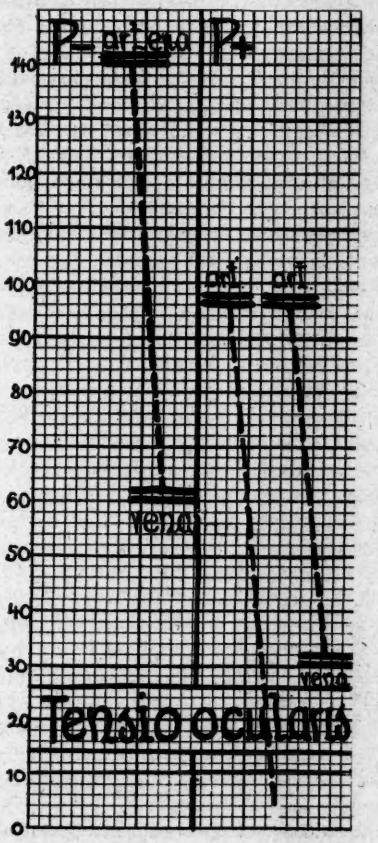

FIG. 1.

Suction-pressure exerted on the bulb of the eye by ophthalmodynamometer in mm. of mercury, which elicited the first arterial or venous pulsation respectively. P−: non-pulsating cases, P+: spontaneous pulsating cases.

evaluating these data: Kukan explains his method so that when he exerts suction on the sclera by the disk, the rim of it presses the bulb of the eye in the same ratio, and thereby the intra-ocular pressure is increased in such a degree, that it surpasses the pressure prevalent within the vessels and thus causes pulsation within the same. Lately Dubois and Fischer from Weve's clinic (*Ophthalmologica*, 1941), proved that the intra-ocular pressure is not increased by this suction method, but the stretching of the sclera changes and the pressure of the retinal vessels decreases below the intra-ocular pressure thereby, and then pulsation ensues in them.

The other difference between the two groups is, that with non-pulsating cases the incidence of ophthalmological complications is 24 per cent. while in pulsating cases it is 12 per cent.

The difference between the two groups, namely, that the drop of pressure with pulsating cases is greater between the arterial and venous part of the retinal circulatory system than with the non-pulsating, and that the entire pressure-level of the latter is shifted higher and that incidence of retinal complications is only half with pulsating eyes as with non-pulsating, each follows from the other. The fact that arterial pressure is established at a higher level signifies that an obstacle prevails with the capillaries, to overcome which the pressure of the central retinal artery is increased. If again pressure is higher within the vein, that means worse circulatory conditions than when spontaneous pulsation prevails, because then the drop of pressure between artery and vein is higher and therefore circulation is more continuous. The following cases serve as instances:

1. Plesh curve of very large amplitude, high blood-pressure, spontaneous retinal venous pulsation absent, severe alterations of the fundus, nephrosclerosis.

2. A curve completely similar to the first, similarly increased high blood-pressure, spontaneous pulsation, intact fundus.

3. Curve of large amplitude, high blood-pressure, spontaneous pulsation, fundus haemorrhage and retinitis foci, complete restitution.

The presence of spontaneous venous pulsation with the two latter cases evidently signifies satisfactory capillary circulation and secures retinal supply and disposition for improvement, while with the first case despite high blood-pressure the circulation of the fundus is bad, because the level of the venous pressure is also increased, thereby the terminal points of the pressure-drop converging, the circulation becomes imperfect.

What about hypotonic cases established at a lower level of pressure? As long as the terminal points of the circulatory system show a difference of physiological pressure-drop, which keeps intact circulation going, this latter functions without trouble. But if this drop of pressure decreases, be it by further decrease of arterial pressure or increase of venous, the circulation becomes worse, as with those

hypotonic cases showing spontaneous venous pulsation because this augments drop of pressure. According to Lauber and Sobansky ocular tension is significant with such hypotonic individuals regarding retinal circulation its relative increase already inhibiting retinal blood circulation. Our own investigations have not demonstrated any difference between hypertonics and hypotonics, pulsating and non-pulsating patients regarding ocular tension. According to Nakayima's experiments, persons using steam baths show a decrease of brachial diastolic pressure without exception, on account of the dilatation of the peripherial small vessels, similarly the diastolic pressure of the central retinal artery decreases, so that spontaneous arterial pulsation ensues and in the majority of cases even venous pulsation becomes evident, the system establishing a lower level of pressure, but ocular tension does not change in the course of the whole process. Normal ocular pressure evidently proceeds parallel to sudden increase or decrease of blood pressure, but not in ratio to continuously developing slow alteration of pressure.

Regarding the peculiarities of spontaneous venous pulsation or the artificially elicited one, venous pulsation elicited by pressure is characterized as already described by Fritz, by sudden increase and stop, according to Fritz a sign of satisfactory capillary permeability and suitable flow, or it increases gradually and slowly.

Or pulsation shows a fine vibration during the whole time, a transition towards that group, where no venous pulsation can be elicited because either capillary circulation is bad or diastolic pressure of the veins increased. Elicited diastolic pulsation of the vein appeared always preceding diastolic pulsation of the artery, and it subsided usually near arterial systolic pulsation ceasing, exceptionally near the cessation of diastolic pulsation.

Spontaneous venous pulsation occurs in 40 per cent. on both sides, 28 per cent. on the right and 32 per cent. on the left eye. Its origin is due, according to Serr, to undulations of the ocular tension synchronous with the revolutions of the heart, ocular tension surpassing venous pressure during systole, and causing compression of the vein. This phenomenon was very clearly visible in cases when the central retinal artery pulsated also and the pulsation of the central retinal vein had not yet ceased: the collapse of the vein exactly coincided with the systolic dilatation of the artery. Of course under pathological conditions there is the possibility of a penetrant venous pulse originating. (Aortic ins., Basedow's disease, cranial tumour). In 10 per cent. of the cases spontaneous pulsation disappears if the patient lays down, as a proof that by increase of intracranial pressure it increases within the vein also and thus surpassing intra-ocular pressure the pulsation ceases, as has been described by one of us already, 1938. (Weinstein: *Brit. Jl. Ophthal*, 1939, p. 396). In 18 per cent. of the cases besides the pulsation synchronous with the

cardiac revolutions, a second separate rhythm of the vein, a formal allorhythmia is discernible, consisting of a ceasing of the rhythmic pulsation for seconds, frequently 4 to 5 then re-appearing again and being replaced by the original rhythm. Then after shorter or longer intervals, a pause again follows. This phenomenon (pulsus intermittens venosus retinae, Fig. 2), has not been described in human

FIG. 2.

Pulsus intermittens spontaneous venosus retinae

ophthalmological physiology and pathology, it has been observed only in dogs as irregularly appearing temporary pulsation and was explained by undulations of tone in the blood-vessels. This intermittent pulsation observed by us, is probably also related to changes of tonicity of the capillaries and is apparent chiefly with vaso-neurotic individuals (migraine, epilepsy). As a practical consideration it follows, that investigating spontaneous venous pulsation the patient should be in a sitting position and the observation should be extended to at least one minute, observing the central retinal vein, because in the prostrate position pulsation frequently it is not visible and often ceases for seconds. With all our cases spontaneous venous pulsation disappeared if the eye was massaged, because then the ocular tension ceased and sank below venous pressure, whereby pulsation ceased for a time. (Seidel and Serr).

Summary

Individuals showing spontaneous venous pulsation have a higher drop of pressure between arterial and venous systems of retinal circulation compared with persons without pulsation, and consequently retinal circulation of the former is more satisfactory.

The level of arterial and venous diastolic pressure values of the fundus of individuals showing no spontaneous venous pulsation are established at a higher level than those of the pulsating group, a circumstance pointing to a circulation inhibited to a high degree within the capillaries.

Retinal complications show an incidence twice as high with cases without pulsation as with those pulsating.

Spontaneous venous pulsation disappears in 10 per cent. of the cases if the patient is laying down, and is of intermittent character in 18 per cent.

Spontaneous venous pulsation disappears if the bulb of the eye is massaged.

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ANNOTATIONS

Moorfields, Westminster and Central Eye Hospital and The Ophthalmic Institute (University of London)

The amalgamation of these three hospitals marks the beginning of a new era in the development of hospital services for eye disease in London. Implicit in this development lies the certainty of greatly improving the teaching and training of ophthalmologists and also the possibility of intensive research into the many unsolved problems of ophthalmology.

More than twenty years ago a scheme for the amalgamation of Moorfields and the Central Eye Hospital was discussed. Some of the preliminary work was done but the scheme failed because it was not thought possible to raise the necessarily large amount of money that would have been required to construct an entirely new hospital with the facilities and equipment then envisaged. This was all the more regrettable as at that time a vacant site adjacent to the Central was available which would have been amply large enough for the projected hospital and still leave space over for such development as the future might require.

Once this scheme was abandoned Moorfields proceeded to reconstruct itself on the very cramped site and the Central—then in a completely new building—just carried on. But in reality neither hospital was quite happy. Moorfields remained cramped and the Central soon found that its new building was not adequate to accommodate the new types of apparatus and the new departments which the developments of the science and practice of ophthalmology made necessary. One has only to mention such things as the slit-lamp, orthoptics, light and X-ray treatment to show what expansion was necessary. A further problem was the training of ophthalmologists. Post-graduate teaching of ophthalmology became an

urgent matter with the institution of the D.O.M.S. and the necessity to accommodate a large number of students added to the congestion. That was the position up to the beginning of the war of 1939/45. During the war it was realised that extensive changes would have to be made if post-war requirements were to be adequately met. In addition to all this it had long been felt that there should be a research institute for ophthalmology with all the requisite laboratories and equipment.

The termination of the war brought a great increase in the number of students and with the conditions prevailing on the continent of Europe it is to be anticipated that their number may increase still further, while the much reduced working hours of the nursing staff added to the difficulties in running the hospitals.

Then came the new Health Act. The Government found itself faced with an inadequate number of ophthalmologists to provide the services for which it had made itself responsible. The result of all this was that Moorfields and the Central agreed to amalgamate and to pool their resources and the University of London undertook the establishment of a teaching institute as part of its general Post-graduate work.

At this stage the Royal Westminster Ophthalmic Hospital decided to join the new amalgamation and in pursuance of these objectives an Act of Parliament was obtained which became operative on January 1st, 1947, establishing the new hospital under the somewhat clumsy appellation which heads this note.

At the present moment the intention is to transfer the hospital services—in-patient and out-patient—of the Central to the other two branches of the combined hospital and to transfer the main laboratory and teaching facilities (pathology, bacteriology, lecture rooms, museums, libraries, etc.), from the other two to the Central which will beco me one of the constituent institutes of the Post-graduate Federation of the University of London. On the one hand this will centralize the routine clinical work in two buildings instead of three without the loss of beds or clinical facilities, and on the other it will free the building of the Central for systematic teaching and research. In this way it is hoped to improve the post-graduate teaching of ophthalmology in London and to start a central research institute which it is hoped may be not without influence on the progress and development of our subject. Nor is it the intention that develop ment stops at this stage. Neither Moorfields nor the Westminster is an ideal building for the modern practice of ophthalmology; the Central is not structurally designed for an institute of teaching and research. Moreover two separate hospitals, although intimately associated, and a research institute geographically divorced from them cannot be considered adequate as a permanent policy. The present arrangement is therefore accepted as the best that can be

accomplished in the immediate future; but the long-term plan when facilities are available is to build a new eye hospital and institute in the University area in close association with University College Hospital—which it is hoped will serve as a general hospital—and University College with its Department of Medical Sciences and its scientific laboratories.

On Eye Shades

We confess that we have always classed the eye shade and the eye bath as household domestic appliances. We would not wish to imply that either is *the* domestic remedy, for in Victorian times this term nearly always denoted the brandy bottle; and we have known the case of a rigid and semi-fainting teetotaller immediately recover when it was suggested in all kindness that she should have "a little drop of brandy."

But if an eye has to be irrigated, an undine, or if none be available, a small tea-pot, is a much better appliance to use than an eye bath; so in most instances we consider a pair of goggles or a pad and bandage to be preferred to an eye shade.

The simplest form of the latter is a D-shaped piece of stiff paper provided with string or tapes to fix round the head. The flesh coloured variety, made of celluloid, one buys at the chemist, deceives nobody and is a potential source of danger. We recall the case of an elderly gentleman who was wearing one and stopped to light a cigarette in the street. His shade caught fire and a nasty superficial burn was the result. Those shades made of black plaited straw seem to us safer and on the whole less unsightly.

There is one state of affairs when an eye shade is a most useful adjunct and that is in diplopia. We cannot speak from personal experience in this instance for we have never suffered from this disability, but if we ever do we shall make a shade out of the best material available at short notice.

When a patient wearing a shade comes up to the desk at which you are seeing out-patients there is no knowing what it may conceal. Anything, from a stye to a severe burn or wound of the eye-ball may be hidden by it, or even an empty socket. It is surprising how often, when the shade is removed, the condition it has concealed from view turns out to be some extremely mild affair, such as a stye. But for ourselves we have to admit that we always experienced a queer feeling of doubt (or shall we say apprehension?) that we never experienced with an open eye, however inflamed it might be. The dread of the unknown is always in excess of the reality.

BOOK NOTICES

An Introduction to the Prescribing and Fitting Contact Lenses. By FRANK DICKINSON, F.B.O.A. (Hons.) F.A.A.O., and K. G. CLIFFORD HALL, F.S.M.C., F.A.A.O. Published on December 30, 1946, at 2 guineas net.

Contact Lenses are much in the public eye at present, and, in a fair proportion of cases, also in their eyes—though for varying, and sometimes rather short periods of time. The appearance of this book is, therefore, to be welcomed, particularly as the authors, though not medically qualified, have had a large experience in fitting these lenses. In such work, nothing can replace actual experience, and it is stated in the preface that the authors are attempting not so much to teach contact lens fitting, as to outline the principles upon which the practical technique is founded. In the same way, as one cannot learn, say anatomy without dissection, so one cannot learn contact lens fitting without actually doing it—but a reference book is undeniably useful by providing guidance, without which progress may become lamentably slow. The guidance provided can best be appreciated by a list of the chapters, which deal successively with the history of contact lenses, their sphere of utility, the types in use and their optics. Then come chapters on the preliminary investigation, theoretical, chemical and psychological fit, with a final chapter on the ethics of practice and the future of contact lenses. There are appendices dealing with contact lens trial sets, extracts from case records, and contact lens terms and abbreviations.

The book is admirably illustrated, with numbers of photographs which show clearly the various techniques for inserting and removing contact lenses, and also some coloured illustrations of the fluorescein method for determining fit. In this connection the authors emphasise the importance of corneal clearance—*i.e.*, of avoiding contact between the back of the lens and the front of the cornea—and of the avoidance of bubbles. They also give details of the various solutions to be used for filling the lenses, prior to insertion. If the new type of lens with a ventilating hole is used, however, all this is changed, because the lens is put in dry, there is capillary contact between it and the cornea and the presence of bubbles is a definite advantage in preventing Sattler's veil. It is not fair to criticise the authors on these counts, however, because the paper describing the new lens is too recent for inclusion in their book, which, in the opinion of the reviewer, is an excellent *ex parte* statement of the uses and properties of various types of contact lenses. Its detailed perusal can certainly be recommended to any who entertain the idea of fitting contact lenses, and wish to know the scope and indications for these appliances. The actual fitting will probably always remain an art, rather than a

science, in the same way as sculpture or painting, but, inasmuch as the sculptor or portrait painter is helped in his work by a knowledge of anatomy, so is the contact lens fitter helped by a knowledge of the scientific background of his art. This knowledge is supplied in full measure by the volume under review.

Principles of the Contact Lens. By H. TREISSMAN, M.B., B.S., *F.R.C.S., D.O.M.S., and E. A. PLAICE.* Price, 10/6 net.

This small volume is designed as a guide to ophthalmologists in the prescribing of contact lenses, and technical details of fitting are omitted. A concise account is given of those optical principles which apply to contact lenses, so that the advantages of these appliances can be fully appreciated. The indications are listed, and the various types of lenses described. A description is given of the preliminary test which should be carried out by the ophthalmologist, and the book ends with some discussion on tolerance. It is well arranged and clearly written, and will be very useful to ophthalmic students, while many practising ophthalmologists will read it with profit.

Report on Defective Colour Vision in Industry. By a Committee of the Colour Group of the Physical Society. Taylor and Francis, Red Lion Court, Fleet Street, E.C.4. Price, 3/6.

Colour vision tests have long been compulsory for occupations in which defective colour vision might prove positively dangerous to life, *e.g.*, the Royal Navy, the Mercantile Marine, and railways. It has been well known, of course, that there are many occupations which cannot be carried out efficiently by colour-defective people. There has, however, been no organized effort to prevent such people from entering these occupations, and such effort could indeed only have been organized after a preliminary investigation of the problem. This has now been excellently done by a committee of the Colour Group of the Physical Society. The presence of Messrs. J. H. Shaxby, W. D. Wright, and F. H. G. Pitt on this Committee is an assurance that the scientific aspects of Colour Deficiency were adequately represented.

The report gives first a brief and accurate account of the nature and incidence of Defective Colour Vision. This is followed by a very useful description (with bibliography) of practically all the colour vision tests in current use. The concluding sentence of this section conveys a salutory warning: "It may be stated that no one test, other than the very expensive colorimetric apparatus is capable of detecting defective colour vision with absolute certainty, but that this certainty may be more nearly approached if more than one type of test is used."

The third chapter records the results from exhaustive enquiry

from trade associations and individual firms upon the extent to which deficiencies affected the work of employees. Many of the industries involved are self-evident; *e.g.*, textiles (dyeing and matching), drapery, lithography and photo-engraving, paintmaking, and so on. Others, less obvious, are equally important, *e.g.*, colour-coding of wires and resistances in electrical industries, heterochromatic photometry—likely to be still more important with the introduction of fluorescent lamps, analytical chemistry and the determination of the end points of titrations and the use of indicators, and so on.

Two factors account for the apparent apathy of industrialists in this matter. In the first place many of the workers are women, and colour deficiency is relatively very rare among women. The second is that in most of the trades a colour defective employee can easily be transferred to some other job.

The remedies recommended by the Committee are school and pre-vocational testing of colour vision.

They recommend that "all children should be tested at school at the age of 13 or over, using one of the approved Confusion Chart Tests." They do not shirk the fact that this is a large order. The evidence of Dr. Gale of the Board of Education, shows how difficult it would be for anything like an adequate test of colour vision to be included in the present system of medical examination. Any single test, as the Committee itself states, is an insufficient criterion, and as much harm as good might well be done by labelling pupils as normal, only to find that they subsequently fail for the Navy or Mercantile Marine. Any group test is likely to prove fallacious. The Collins-Drevor Test with Bradley papers has been used, and "nearly 78 per cent. of boys and over 94 per cent. of girls who failed in the examination quoted proved to have no colour deficiency when tested individually by the Ishihara Charts.

Pre-vocational tests are far more practicable and are to be strongly recommended. Their value has indeed been proved in Edinburgh and Glasgow. The Committee say: "In view of the very general acceptance of confusion chart tests, and because they are in fact suitable for a great variety of industries and trades, we recommend their use as a good all-purpose test. But we also recommend that they should be supplemented by a trade test designed for the particular kind of task which will be undertaken under normal working conditions."

The Science of Seeing. By IDA MANN and ANTOINETTE PIRIE. Pp. 220, with 8 illustrations. Pelican Books (A.157). 1946. Price, 1/-.

As "Madam How and Lady Why" was written by Charles Kingsley as a book of first lessons in earth lore for children, so the present booklet may be likened to a series of chapters on eye lore

for those who have not been initiated into ophthalmology. It is extraordinary how little even educated people know about their eyes: many do not even know the difference between an oculist and an optician. There was a need for a book of this sort, in which the writing is easy and the style at times colloquial, addressed to the great mass of the population.

Certain widely spread erroneous ideas about eye work being harmful to the eye, glasses tending to weaken the sight and that it is possible to take the eye out, scrape it and put it back again are demolished, and the reader is conducted up the zoological staircase from the reaction of the amoeba to light to vision in the human species.

In discussing myopia the authors say that we know of no means of checking the growth of the child, but if they will refer to Nicholas Nickleby they will find that Mr. and Mrs. Crummles put the infant phenomenon on to an unlimited allowance of gin and water from infancy in order to keep her small. Perhaps this idea needs to be demolished with the others.

Many interesting facts emerge from these pages. Bulls are colour blind and it is not the red cloak that irritates them, but more probably the movement. Bees do not see red; wasps are not mentioned, but the small urchin who pokes a stick into a wasp's nest might disagree as far as wasps are concerned. Seals are highly astigmatic. We congratulate the authors most heartily. The chapters are all good, especially those on colour vision; vitamins and vision; things that may go wrong with the mechanism of seeing; things which may affect the function of the eyes, apart from disease and injury; what the blind can do and how they can be taught.

All those of Victorian status will appreciate the reference to the use of a stereoscope on Sunday afternoons combining amusement with latent instruction.

With regard to the limerick on page 80 we do not claim to be a Hampshire Hog, but would suggest that the village of Cosham in that county would rhyme better with "wash 'em" than East Bosham. We were under the impression that the latter was pronounced "Boseham".

CORRESPONDENCE

MYOPIA AND PSEUDO-MYOPIA

To the Editors of THE BRITISH JOURNAL OF OPHTHALMOLOGY.

DEAR SIRS,—I desire to support Mr. Lavery in what he has said in your last issue on "Myopia and Pseudo-myopia" by Mr. Spencer Walker and I should like to go a step further.

His letter has particularly brought home to me the case of a young man who came to me the other day complaining that he had been rejected in the visual examination for the Master Mariner's Certificate. When he first consulted me a few years ago he was accompanied by his father. I explained to him that though his son would probably pass his entrance examination I was afraid that he would not pass his final because his myopia would most likely have increased by that time.

Now my point is why should such a healthy young man with excellent colour vision and with only a slight amount of myopia, be lost to the services of the Mercantile Marine or even to the Navy, but be acceptable to the land forces. It seems to be perfectly correct for an Admiral or a Sea Captain to view a ship in the offing by means of a pair of binoculars but incorrect for him to do the same thing with a pair of glasses poised on his nose.

Our Faculty of Ophthalmology should endeavour to educate the powers that be to a more sane and reasonable outlook on these matters. Many a worthy Son of the Sea whose ancestors have played their part in making England great has been cast aside as worthless because he had half a dioptre of myopia.

I think the whole subject of myopia merits careful and serious consideration. Is it wise for the M.O.H. to insist on the refractionist getting 6/6 or 6/5 vision with minus glasses or would the pupil have been better treated if his 6/9 vision had been untouched and plus glasses with base in prisms been prescribed to assist his accommodation and convergence?

Yours faithfully,

FRANCIS E. PRESTON

44, QUEEN ANN STREET, W.1
25th February, 1947

REMOVAL OF THE WRONG EYE

To the Editors of THE BRITISH JOURNAL OF OPHTHALMOLOGY.

DEAR SIRS,—It was with great interest that I read, in the January issue of the Journal, the interesting article by Dr. H. M. Traquair, concerning the removal of the wrong eye. May I offer a safe and simple method to the profession to avoid this mistake, and may I be allowed to correct a linguistic misinterpretation in this article?

The misinterpretation was due to the translation of the "Soll" in Elschnig's quotation. The "Soll," is equivalent to the Latin "Dicitur" and does not mean that this case has actually occurred; it means that it was said (by someone) that the case has (somewhere)

actually occurred. Thus, Elschnig himself did not experience this mishap neither did it occur in his department—at least not between 1912 and 1932, to my knowledge.

My suggestion is to cut the lashes of every patient's eye to be operated on, the day before the operation, or even two days previous to the operation. This can be done in the ward or in the surgeon's office where all records are easily available and when—in the worst case—the patient may remind the assistant that he is preparing the wrong eye. In Elschnig's clinic, we used to cut the cilia in the preparation room adjacent to the operating room; for the last years, I have been cutting the lashes one or two days before surgery, in all intra-ocular operations. The same procedure could be adopted for the enucleation and will prevent the search for, and possible mistake of, the eye to be operated on.

With sincerest congratulations for the improved appearance of the Journal.

I remain, very truly yours,

K. W. ASCHER, M.D.

2508, AUBURN AVENUE,
CINCINNATI 19, OHIO,
February 28, 1947.

OBITUARY

SIR ARNOLD LAWSON, K.B.E.

SIR ARNOLD LAWSON was the fourth of seven sons of George Lawson (1831-1903). George Lawson was a pupil of Sir William Bowman at King's College Hospital, and went to the Crimea as an Assistant Surgeon in 1854. In May, 1855, he had a very severe attack of typhus fever that produced a complete paraplegia, and he was invalided out of the Army in January, 1856. He was already an Assistant Surgeon at Middlesex Hospital where he was a colleague of John Whitaker Hulke. George Lawson was elected Assistant Surgeon to Moorfields Eye Hospital in 1862 on the same day as Sir Jonathan Hutchinson.

He became Surgeon-Oculist to Queen Victoria, holding this appointment until her death in 1901.

He was a man of great charm, a Tractarian, deeply religious, whose generosity, especially to his hospital patients, has become legendary. To follow such a distinguished father is a heavy task, and this Sir Arnold did in detail except that he confined the professional side of his life to ophthalmology.

He was born at 12, Harley Street (into which his father had moved in 1863) on December 4, 1867, and he was destined to spend his whole life there. He was educated at the Merchant Taylors School and in 1886 entered the Medical School at Middlesex Hospital as Senior Entrance Scholar. He did well as a student, winning the Hetley Prize in 1890 and was Senior Broderip Scholar in 1891, in which year he qualified. He graduated as M.D. of Brussels in 1891 and obtained his F.R.C.S. diploma in 1893.

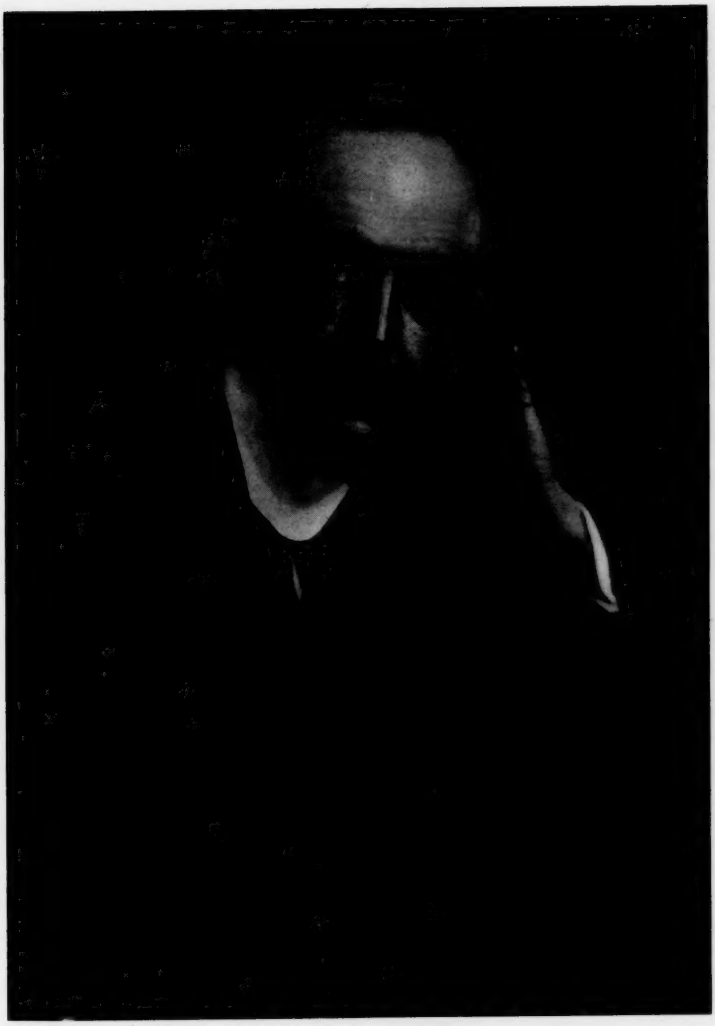
Sir Arnold soon decided to be an ophthalmic surgeon and joined his father in practice. He was elected ophthalmic surgeon to the Paddington Green Children's Hospital in 1896 after having worked with Sir John Tweedy at Moorfields. In 1900, when it was decided to increase the visiting staff at Moorfields from nine to twelve, he was elected Assistant Surgeon together with John Herbert Fisher and Percy Flemming. He became full surgeon in 1907 and retired in 1914, becoming Consulting Surgeon in 1923. In 1910 he joined William Lang at Middlesex as Assistant Surgeon, succeeding him as full surgeon in 1914. In 1932 he was elected Consulting Surgeon. He served as ophthalmic surgeon to the Hospital of St. John and St. Elizabeth, and from 1914 to 1919 was ophthalmic surgeon to King Edward VII Hospital for Officers. For many years up to the time of his death he was Consulting Ophthalmic Surgeon to the Royal Hospital for Incurables at Putney and to the Royal Medical Benevolent College, Epsom.

In 1914 began his important work in connection with the founding of St. Dunstan's. He became principal ophthalmic adviser to Sir Arthur Pearson in this connection and remained Chairman of the Ophthalmic Advisory Committee until his death. For this work he was appointed K.B.E. in 1920.

In 1940 he was appointed Ophthalmic Consultant to the Navy. Of this he was very proud, refusing to take any fee for his services, saying that it was his contribution to the branch of the Forces in which his son served.

He became suddenly ill in 1918 and the nature of the complaint was not diagnosed. He recovered almost as suddenly but in July, 1921, the true nature of his ill-health became apparent when he had a serious breakdown and he spent six months in a sanatorium. After his return to work he gave up many of his appointments and for five years attended no meetings where many people were congregated. He seemed to have recovered all his vigour so as to lead a busy life to the time of his death on January 19, 1947. He actually saw patients on December 19.

Sir Arnold became a member of the Ophthalmological Society in 1896 and after serving as a Vice-President became Treasurer in 1919, retaining the office until 1947 (when he was elected honorary



SIR ARNOLD LAWSON—1867-1947

member), so that his resignation and death were reported at the same meeting of the Council. In this post he was very successful and the work interested him. He always said he hoped to hold the post for thirty years.

He became president of the Royal Medical Benevolent Fund on the death of Sir Thomas Barlow, and in this position proved a great success. His appeals, more especially the one at Christmas produced much greater funds than previously. He collected large sums for the completion and decoration of the Chapel at Middlesex Hospital in which his father and family had always taken a generous interest.

Lawson's literary output was not large when one considers the length of time he was in practice. He edited and largely re-wrote his father's text-book on Diseases and Injuries of the Eye, in 1903. He published a report on the War blind at St. Dunstan's in 1920; and wrote articles in Latham and English's System of Treatment. He published with Sir James Mackenzie Davidson a monograph on Treatment of the Eye by Radium.

He attended meetings of the Ophthalmological Society and the Ophthalmic Section of the Royal Society of Medicine, which he served as president from 1924 to 1926, taking part in discussions and occasionally reading papers.

Lawson will be much missed, especially by his older colleagues. He was a well known figure to all, as he appeared every year for so long a time at the annual meetings of the Ophthalmological Society to present the treasurer's report.

The funeral took place at All Saints Church, Margaret Street, in the presence of a large representative congregation. He had been connected with All Saints from his earliest years and claimed to have been one of the oldest members of the congregation. He had displayed as a boy his love of music, and especially of church music. He was a regular member of the congregation at the Sunday early services.

He married in 1904, Helen, daughter of Andrew Clark, F.R.C.S., of 71, Harley Street, who was a surgeon to the Middlesex Hospital. She died in 1944 and they are survived by two sons and a daughter.

DEWAN BAHADUR DR. K. KOMAN NAYAR

WE regret to announce the death of Dewan Bahadur Dr. K. Koman Nayar, D.O.M.S. at his home in Madras, on November 1, 1946. Dr. Koman Nayar was one of the leading ophthalmologists in India. He served at the Government Ophthalmic Hospital, Madras, in various capacities from 1912 to 1946 when he retired. He became assistant superintendent in December, 1918, and frequently acted

as superintendent, until in 1938 he was confirmed in that post, and appointed Professor of Ophthalmology, Medical College, Madras. His courteous unassuming manner and devotion to duty were combined with a professional ability and sound judgment appreciated by all who came in contact with him.

NOTES

Hunterian Lecture

MR. J. MINTON'S Hunterian Lecture on "Occupational Eye Diseases and Injuries" will be given at the Royal College of Surgeons on June 12, 1947, at 5 p.m.

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Oxford Ophthalmological Congress

THE 33rd Annual Meeting will be held at Oxford on July 3, 4 and 5, 1947, in the Department of Human Anatomy. The programme includes a discussion on "The Contracted Socket," to be opened by Professor T. Pomfret Kilner and Mr. H. B. Stallard. The Doyne Memorial Lecture will be given by Professor L. S. Stone, of Yale University. His subject is the "Return of Vision and Functional Polarisation in the Retinae of Transplanted Eyes." Arrangements are being made for a museum of exhibits.

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Irish Ophthalmological Society

THE next General Meeting of the Irish Ophthalmological Society will be held in Dublin on May 22 and 23. Prof. Bernard Samuels of New York will deliver the Montgomery Lecture on May 22.

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The Illuminating Engineering Society

LIGHTING IN COAL MINES, by J. Ivon Graham, M.A., M.Sc., M.I.Min.E. (Summary of a Paper to be given at a Meeting of the Illuminating Engineering Society to take place at the E.L.M.A. Lighting Service Bureau, 2, Savoy Hill, London, W.C.2, at 6 p.m. on Tuesday, March 11, 1947).

INTRODUCTION. The paper opens with a reference to the report issued in 1944 by the Technical Advisory Committee appointed by the Minister of Fuel and Power under the Chairmanship of Sir Charles Reid which stated that "no man can work properly without good light, and this especially so when conditions are difficult."

The amount of light given by early forms of safety lamp was very low and it is only the capacity of the human eye to adapt itself to low illuminations that enables the miner to do any appreciable work. Mention is made of attempts to improve lighting conditions in mines over a number of years. Although the installation of mains electric lighting or of pneumatic electric lamps has not shown anything definite as regards increased output it has led to a reduction in accidents.

PORTABLE AND CAP LAMPS. Two electric hand lamps were in use prior to 1913 but it was not until 1934 that there was any real improvement in the illumination given by hand lamps. The problem of glare then arose and the soft yellow light and the reduced glare of the improved flame lamps giving 4 candle power was often preferred to the use of electric lamps.

Tests carried out on the maximum candle power given by oil and electric lamps both before and after the shift are mentioned. Suggestions are made by which the best possible utilisation of energy from the battery of electric lamps might be obtained.

Cap lamps giving a higher illumination have become more popular during the last few years and have the additional advantage of reduced weight and freedom of movement of the hands.

The Reid Committee recommended an illumination standard of the order of 0·4 ft. candles in the general working area though it was appreciated that such a standard was impossible with either the hand or cap lamps. Even if, with improvements in the candle power/weight ration, the illumination given by cap lamps may give the necessary local illumination, the absence of general lighting would still be a drawback.

ILLUMINATION BY MEANS OTHER THAN PORTABLE LAMPS.

(a) *Transportable Self-contained Battery Lamps.* Lamps of this category were the logical development of the miner's hand lamp. The advantages are that they can be readily moved to where required and that illumination of the required standard can be provided on the work. On the other hand there is the nuisance of daily charging, difficulty in obtaining a flame-proof certificate, transport to and from and need of care at the working face and finally the glare produced.

(b) *Mains Lighting.* Mains lighting is now permitted subject to special regulations. A number of trial installations and tests which have been carried out are described. Mains lighting in the Ruhr coalfield, where it is reported the illumination in mines is of a high standard, is also discussed.

LAMPS FOR MAINS LIGHTING. The characteristics of the various types of lamps, e.g., tungsten, mercury, sodium, etc., are

mentioned. Fluorescent tube lighting has distinct advantages including the psychological effect of daylight, high efficiency and low brightness, and the application of this system of lighting is now being developed through a Committee of the Ministry of Fuel and Power and with the assistance of the National Coal Board.

THE PNEUMATIC-ELECTRIC LAMP. Conditions in many pits may not permit the application of mains lighting even with relaxation of the present regulations. Such pits, if equipped with compressed air, have in the pneumatic-electric lamp a means ready at hand for greatly increasing the illumination at the coal face. This lamp is described in some detail together with the cost of operation. The application of vapour-discharge sources and the fluorescent tube to this lamp is also described.

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Corrigenda

UNFORTUNATELY authors' proof corrections of the paper in our last issue by Professors L. C. Martin and R. W. B. Pearse had not been received when the number went to press. By an oversight the horizontal scale numbers were omitted in Figs. 3 and 4. The entire logarithm scale shown in the squares starts at $\bar{2}{\cdot}5$ and ends at $1{\cdot}0$ reading from left to right. In addition the following errors should be corrected: p. 131, last line but one, The acuity object (Fig. 1) should read The acuity object (S, Fig. 1.). P. 135, Table III, degree signs should be added in each first compartment of the six columns as follows; 3°/61° and so on. Page 137, Filters. The 'm' in Ilford minus Green should have been a capital. In No. 8, delete (γ): in No. 10 the last half of the parenthesis should be added. Page 138, Table IV. In Ilford Minus Green column, the 18th figure should read 3·06, and in the same table, 2nd line, last column, 0·772 should read 0·77. Page 142, Table VI, 1st line, last column, 0·066 White should read 0·063. Page 144, the final word of the first paragraph should read tests not texts. At the end of the paper the following sentence should be added. "Our thanks are due to many observers who took part in the trials; and to the Director of Research, Admiralty, for permission to publish this report."

IN the paper on "Posterior ring abscess of metastatic origin in Behcet's Disease" (by A. Feigenbaum and W. Kornblueth), December, 1946, p. 729, para. 1, line 9, for "general" read "genital."